SEP 2 1913

VOL. CXLVI, No. 3 SEPTEMBER, 1913 No. 498

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES

EDITED BY GEORGE MORRIS PIERSOL, M.D.

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THE

AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

SEPTEMBER, 1913

ORIGINAL ARTICLES

A LOBAR FORM OF BRONCHOPNEUMONIA OF LONG DURATION, OCCURRING IN CHILDREN AND YOUNG ADULTS.[1]

By David Riesman, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

For some time, possibly four or five years, I have been interested in a disease of the lungs which cannot be readily classified nor easily named.

Case I.—The first case I saw was in a young girl, who came to the dispensary of the Polyclinic Hospital and puzzled my colleagues and myself by a long-continued, low fever. Week after week on on her visits to the clinic we noted a moderate elevation of temperature, and as she had a cough, was pale and of poor physique, tuberculosis was naturally suspected. But aside from failure to find any evidence in the sputum, the physical signs—an abundance of crackling rales—were strictly limited to one lower lobe, there being no involvement of the apices. The history did not suggest an unresolving lobar pneumonia, and the child, so far as I can recall—the record is now lost—was not confined to bed at any time. After a most protracted course, covering possibly two or three months, the girl recovered completely.

Case II.—On September 12, 1911, I saw in my office Pearl L., a girl, aged thirteen years, who had been coughing for two weeks. At the age of two years she had whooping cough, otherwise she had been well. Although she did not appear to be very ill, I found impairment of resonance over the entire left lower lobe and sharply limited to it. The breath sounds were harsh and of a broncho-

[1] Read at the meeting of the Association of American Physicians, May 8, 1913. A preliminary report was made to the College of Physicians of Philadelphia on February 5, 1913.

vesicular character. There were also numerous crackling rales. The right side as well as the upper lobe of the left lung was entirely normal. Temperature, 99.5°; pulse, 120. Four days later the signs were more marked, the involvement extending from the base of the left lobe to a little above the middle of the left scapula, and from the spinal column to the postaxillary line. The impairment was, however, very slight, and only discoverable by careful comparison of the two sides. The rales were of a coarse, moist type; temperature, 98.9°; pulse, 108. On her next two visits very few rales could be detected. On October 27, six weeks after I first saw her and eight weeks after the beginning of her illness, rather coarse rales confined entirely to the left lower lobe could still be heard. On November 22, no rales could be found, but as late as January 4, 1912, four months or more after the onset of the disease, the breath sounds over the left base were still a little harsh. I saw the girl again February 17, 1912, for some trifling condition, and at that time the lungs were clear.

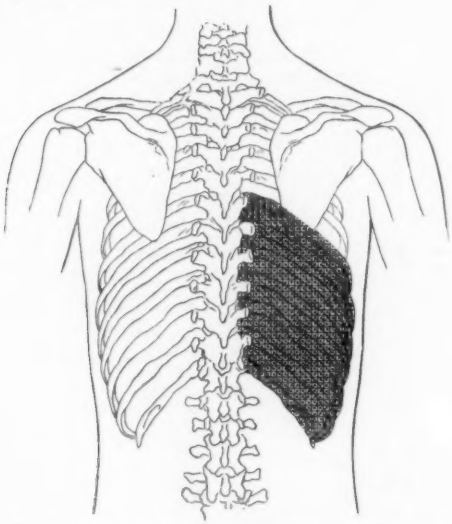

FIG. 1.—Bertha M. Impairment of resonance; bronchovesicular breathing; crackling rales; right lower lobe.

CASE III.—Bertha M., aged nineteen years, a Normal School girl, came to see me March 31, 1911, on account of a severe cough from which she had suffered on and off for three months. She is very robust and comes of healthy stock. The cough had "somewhat run her down," to use her own words. Temperature, 100.5°; pulse, 120. On examination I found impairment of resonance over the right chest from the angle of the scapula to the base. Over this

area the vocal fremitus was a little increased. On auscultation over the entire lower right lobe posteriorly, laterally, and in front from the mammary region down, numerous crackling rales could be heard. The lung elsewhere was normal. (Fig. 1.) The patient had no expectoration, the appetite was diminished, the bowels constipated. By April 8, only a few dry rales remained at the base of the right chest.

CASE IV.—Bernice B., aged six years, had whooping cough soon after birth, a mastoid operation and adenectomy at three, otherwise nothing except slight anemia and transient choreiform movements. I saw her first on May 28, 1912. She had been coughing for some time. On June 6, I noted in my records: Cough very hard; temperature, 99.4°; harsh breathing at left base. On June 10: Cough continues; temperature, 99.4°; slight impairment of the percussion note of the left lower lobe posteriorly and in the axillary region, with harsh breathing and a fair number of fine rales. On June 17 the notes state: Temperature normal; cough less severe; rales have nearly all disappeared.

CASE V.—Dora Y., aged thirteen years, was seen with Dr. Hofkin on June 27, 1912, the history being that she had been ill with a continued fever for some time; just how long I could not ascertain. Typhoid fever and tuberculosis had been suspected. There was no cough; no expectoration; the fever was moderate; at no time had the child seemed very ill. A few weeks before she was taken sick an uncle had died in the same house of lobar pneumonia. Examination of the patient, who was up and about, showed slight impairment of resonance over the entire lower right lobe posteriorly and in the axillary region. The vocal fremitus was not altered. On auscultation a tremendous shower of crackling rales, which became a little finer after coughing, could be heard. Inspiration was harsh and expiration somewhat prolonged, but not bronchial. I ventured the positive statement that the child did not have tuberculosis and would recover fully. In September Dr. Hofkin wrote to me that the girl had been taken to Atlantic City and that he had found the lungs clear five weeks after our consultation, but had noted the persistence of harsh breathing over the formerly affected lobe. When he reëxamined her in September not the slightest abnormality could be detected.

CASE VI.—Sarah R., a girl aged twelve years, was first seen October 20, 1912. For three or four weeks she had had a severe cough, with some expectoration. According to the mother the child had been subject to such attacks for several winters, and when once started they would last throughout the cold season. The cough was worse at night and often disturbed the child's sleep. There were no night-sweats. The family history was good, and as for the patient, aside from the winter cough, she had had nothing except chickenpox at the age of two years. Examination showed

over the left lung posteriorly a slight impairment of resonance. On auscultation numerous dry and some moist rales could be heard over the lower lobe of the left lung, behind and as far forward as the midaxillary region. (Fig. 2.) Nowhere else were any abnormal sounds to be detected. The heart was normal; the spleen not enlarged; temperature, 98°; pulse, 80. A few days later the patient had a severe stitch in the left side with a catch in breathing. When I saw her on October 27, there was no friction sound. The resonance over the left lower lobe was still a trifle impaired; the rales had disappeared.

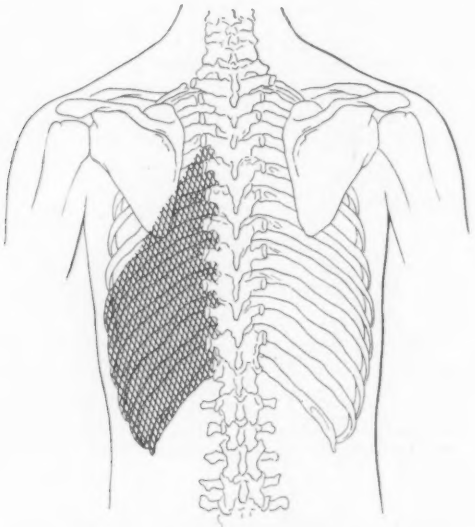

FIG. 2.—Sarah R. Impairment of resonance; bronchovesicular breathing; crackling rales; left lower lobe. Posterior view.

CASE VII.—W. N., a colored lad, aged fourteen years, was sent to me by Dr. Watson, at the Polyclinic Hospital, on March 1 of this year, because, just as he was about to undergo an operation for enlarged tonsils, it was discovered that he had a temperature of 100°. The boy had had diphtheria at the age of seven and frequent attacks of tonsillitis. He did not complain of anything, but after we had detected the physical signs about to be described he admitted that for a week past he had had a slight cough, without expectoration, and some headache. I wish I could picture to you the surprise of my group of postgraduate students—and my own—when upon examination we found over the lower lobe of the left lung many small moist rales, bronchovesicular breathing, and impairment of the percussion note. (Fig. 3.) There was nothing

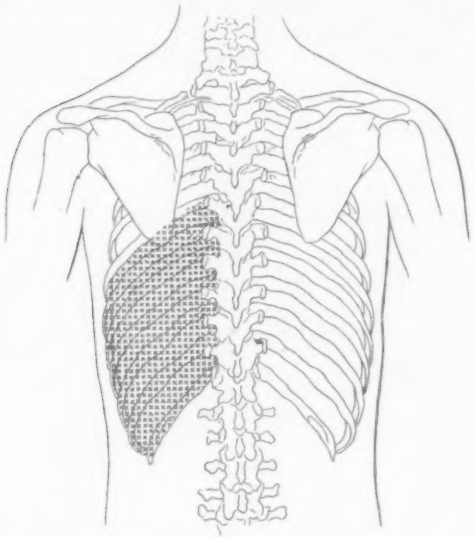

FIG. 3.—W. N. Impairment of resonance; bronchovesicular breathing; crackling rales; left lower lobe.

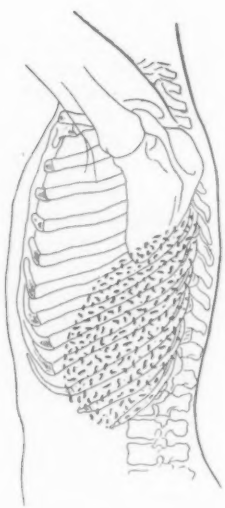

FIG. 4.—Dr. H. Impairment of resonance, bronchovesicular breathing; crackling rales; left lower lobe. Lateral view.

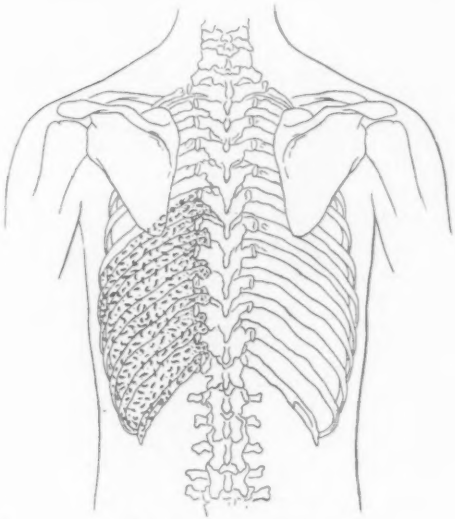

FIG. 5.—Same case as Fig. 4. Posterior view.

in the history, in the symptoms, or in the general impression that the boy made upon us to suggest any trouble in the lung. Had it not been for our practice of making a routine examination of the posterior bases of the lung the trouble would surely have been overlooked. It is not improbable that some of the ether pneumonias are preceded by just such a condition as we found in this boy. If that is true then it behooves us in every case before an operation to make a thorough examination of the back of the chest.

The blood count gave the following results:

Hemoglobin	88 per cent.
Red cells	5,320,000
Leukocytes	16,160
Differential count:	
Polymorphonuclear cells	57.4 per cent.
Mononuclear cells	7.0 "
Small lymphocytes	28.6 "
Transitional	5.4 "
Eosinophiles	1.6 "

At the end of three weeks from the time he was first seen the boy was entirely well.

I have cited the foregoing seven cases as typical of the disease. I have seen perhaps double that number.

PATHOLOGY. There have been no autopsies and no *x*-ray examinations, so that the actual pathological anatomy is an inference. The condition is not an ordinary bronchitis: (1) because it is strictly unilateral, while bronchitis is generally bilateral; and (2) because unlike bronchitis it is accompanied by an impairment of the percussion note and by breathing of a bronchovesicular character. Repeated examination in my cases has shown the physical signs to be quite stationary in the part first affected. Nor can the condition be a pleurisy: the signs remain unchanged, no fluid is demonstrable, the tactile fremitus is either not altered or increased, and the line of dulness follows the slant of the division between the lobes and has not the characteristic curve of an effusion. There is also practically no pain.

It is not a lobar pneumonia of the ordinary type, for it has not the acute, sharp onset, nor does it at any time give the impression that there is complete consolidation of the lung.

The view that we are dealing with a lobular or catarrhal pneumonia becoming confluent and assuming a lobar distribution seems to me to accord best with the conditions present. While lobular pneumonia in the vast majority of cases is a bilateral process, there is no inherent reason why it may not be unilateral. As the modes of infection in the two forms of pneumonia are not unlike; and as the infecting organism is generally the same, it is well within the law of probability that lobular pneumonia may be confined to the same parts of the lung as lobar pneumonia. Since we possess no

satisfactory explanation for the lobar distribution in the one, none can be demanded for a similar distribution in the other.

In some experiments with the pneumococcus, Dr. Kolmer and myself, using the Lamar-Meltzer method, produced in dogs a pneumonia confined to a single lobe that to our minds had the characteristics of a spreading lobular rather than of a true lobar pneumonia, thus bearing a close analogy to the disease under discussion. At best, however, the pathological differences between lobular pneumonia and lobar pneumonia are neither great nor important.

It has not been possible to obtain sputum in many of the cases. When it was obtained it showed chiefly pneumococci. That the pneumococcus is capable of causing not only acute but also chronic pulmonary infections is demonstrated by the painstaking researches of Leutscher.

There is no evidence that the condition is an interstitial pneumonia of the type so ably described by Dr. Jacobi,[2] for it heals without residue—without evidence of retraction.

The disease would not impress anyone as a manifestation of influenza. The cases I have seen were scattered over a considerable period of time. They had none of the catarrhal symptoms nor the prostration so characteristic of influenza. Moreover, no other members of the patients' families were affected.

The chief symptoms are cough and a moderate fever, rarely above 101°, extending over a long period—from several weeks to three or four months. The cough may be harassing, but at times is slight, scarcely of enough moment to attract attention. There may be considerable expectoration or none; it may contain a little blood, but in my experience has never been rust-colored. The physical signs are entirely out of proportion to the symptoms. There is always some dulness, which is most easily detected by a careful comparison of the two sides, and usually extends to the angle or the middle of the scapula. Rales are, as a rule, abundant, and of the peculiar quality best described as consonating. They are moist rather than dry, though both types may be found. In the presence of minor subjective symptoms the listener will often be surprised when approaching the base of the chest to find his ear bombarded by a chorus of exquisitely crackling sounds. The rales are heard best in inspiration, and are often increased by coughing. In the majority of cases the disease involves the lower lobe of the left lung, but this may be a mere coincidence, as the number of cases is as yet too small for a definite conclusion. Girls predominated among my patients. As to age, the majority were between ten and twenty years—one was twenty-seven and one twenty-eight years. All the cases have ended in recovery without a vestige of the morbid process remaining.

[2] Arch. Ped., January, 1903

On looking, not exhaustively, through the literature I find nothing directly bearing upon the subject. A number of authors in their chapters on bronchopneumonia state that at times the disease is most marked in one lobe, and when confluent may simulate lobar pneumonia. Such types are, however, described as exceptionally severe, with high fever, marked dyspnea, profound prostration, and great danger to life. They differ thus radically from the disease with which we are dealing. Beddard[3] speaks of a primary lobular pneumonia which is usually confluent and is diagnosticated as lobar. This, however, has a sudden onset, with high temperature and severe nervous symptoms; the duration is short, the pyrexia is quite regular and sustained, and it often ends by crisis. This, of course, does not correspond to our disease. West[4] described three types of bronchopneumonia, none of which is identical with the one under consideration; although he recognized a secondary bronchopneumonia, not, however, of lobar type, with a protracted course lasting three months or more. The nearest approach is found in Powell and Hartley's book.[5] They speak of a confluent form involving adjacent lobes of a large portion of the lung, sometimes a whole lobe, producing more or less dense consolidation. It may be associated with ordinary bronchitis of catarrhal origin, and very often occurs in the course of whooping cough. They have also met with it in certain cases of heart disease, and as a complication in pulmonary tuberculosis. In none of my cases was whooping cough, heart disease, or pulmonary tuberculosis a factor in the process; moreover, in severity and course the condition described by Powell and Hartley and the one here discussed are very different. Babcock[6] recognizes a confluent bronchopneumonia, but does not go into details regarding the symptoms or course. Wilson Fox does not mention it.

TREATMENT. In the treatment the measures that have seemed to me of some avail are counter-irritation to the chest, abundant feeding, and either a simple cough mixture with a small dose of an opiate, or one of the creosote preparations. Whenever the weather was favorable I advised that the patient be taken outdoors. A sojourn at the seashore in proper season is also beneficial.

The essential features of the condition I have described may be epitomized as follows:

1. The disease is a confluent lobular pneumonia of lobar distribution characterized by long duration, low fever, and the following physical signs: impairment of resonance, bronchovesicular breathing, and showers of crackling rales.

2. It must be looked upon as one of the causes of obscure long-continued fever.

[3] Allbutt and Rolleston's System of Medicine, vol. v, London, 1909.
[4] Diseases of the Organs of Respiration.
[5] Diseases of the Lungs, 1911, fifth edition.
[6] Ibid., New York, 1907.

3. The disease always seems to end in complete recovery both symptomatically and anatomically.

4. In the beginning typhoid fever may be suspected, in the later stages tuberculosis.

5. The disease is, I believe, often overlooked, due to the fact that we seldom examine the lower posterior aspects of the chest in ambulatory cases, especially when the symptoms are rather trivial. I am quite sure the diagnosis of tuberculosis is often made in these cases of chronic cough, with low, continued fever; but if the chest is carefully examined, back and front, above and below, the peculiar, almost specific character of the disease will be discovered, and then the thought of tuberculosis will be no longer entertained.

THE TRUE VALUE OF OPERATION FOR CANCER.

By Edward Milton Foote, M.D.,

VISITING SURGEON TO THE NEW YORK SKIN AND CANCER HOSPITAL.

In order to estimate the true value of operation for cancer, we must know (1) the object of the operation, and (2) its result. It is often assumed that there is only one reason for such an operation—namely, the removal of all diseased tissue. This is the so-called radical operation. Its range has been extended to include not only the visibly diseased tissues, but also those tissues which may have in them seeds of disease for future development, and especially adjacent lymph glands and fascial planes. This side of the subject has been thoroughly studied and its technical applications to the various cancer sites of the body repeatedly described. In fact, it may justly be said to have dominated the surgical mind, determining the type of operation and classifying the results. Important as attempted removal of the cancerous and precancerous tissues may be, this is by no means the only reason for operation in cancer, and it is manifestly an absurdity to follow blindly methods of technique worked out for a radical operation when the possibility of radical operation does not exist. Rather should one shape the operation in each case to the objects to be gained by operation in that particular case.

Speaking broadly, there are four reasons for operation for cancer which may be present in the mind of patient or surgeon:

1. The complete removal of the cancer and cancer-bearing tissue—the so-called radical cure.

2. The establishment of a diagnosis.

3. The relief of some special symptom, such as hemorrhage or discharge from an ulcerating surface, or the closure of a sinus, or the division of a stricture, or the removal of a disfigurement.

4. The attainment of certain social ends—to keep up the patient's hope or to satisfy the family that something is being done, etc.

One is tempted to add another reason, which probably exists in the mind of the patient and his friends oftener than they would like to admit, and that is the possibility that the patient may die from operation. But if this is admitted as a reason for operation, it will take its place among the social ends in class four.

It is obvious that the choice of operation should depend in no small degree upon which of these four reasons exists. The first reason—namely, the possibility of a complete removal of the growth—justly outweighs all other considerations when it is present. In order to accomplish this end the radical operations have been made more and more extensive, with a corresponding increase in operative mortality and postoperative debility. It is manifest that this tendency can be carried too far, that the price paid for possible immunity may be too great, especially in the case of a tumor beyond the earliest stage. The more extensive the growth the more extensive must be the operation, and the greater will be the operative risk, while the chance of a radical cure grows less and less.

The second object for which one may operate in cancer is the establishment of a diagnosis. If the growth is small it may be entirely removed, so that diagnosis and complete removal are effected at the same time. But this double object can only be attained satisfactorily in the case of small growths of limited malignancy, such as beginning epitheliomas of the skin away from the orifices of the body, so situated that it is practical to remove a fair margin of sound skin with the tumor. On the other hand if one removes in this way a small tumor of the breast, and it proves to be a commencing carcinoma and not a fibroadenoma, the requirements of a radical operation will not have been satisfied.

The field of the diagnostic operation has been narrowed in another way. It was once believed that a small portion of a tumor could safely be extracted by a punch or cut out through a small incision and submitted to microscopic examination. Such methods of examination are not looked upon with favor at the present time, certainly not in the earlier stages of a cancer or suspected cancer. The examination of a small piece of tissue may give misleading results, especially in incipient or doubtful cases, where a wrong diagnosis will do the most harm. Furthermore, cutting or punching through the normal tissue planes which surround a malignant growth has in some cases hastened its spread into these new planes, so that this risk has to be considered in such a diagnostic procedure, and it is generally conceded that patients should not be subjected to this risk unless they are beyond the possibility of a radical operation.

Another and better form of diagnostic operation is the exposure of a tumor, the examination of a portion of it by frozen section, and the completion of operation according to the report of the pathologist. Here the risk is that of an added delay of ten to thirty minutes for the pathologic examination. In many cases this is negligible, and the time can be reduced to a minimum, even below that mentioned, with practice in good surroundings. Some have made the claim that this technique exposes the patient to a dissemination of his cancer even though a radical removal is at once carried out. Such an extreme statement is not susceptible of proof and most surgeons have refused to be influenced by it. There are, however, limitations to the method. It should not be employed with patients too weak to endure the necessary delay with safety, and the section should always be removed in such a way that the wound can be properly closed if further operation is decided against. For example, one would not be justified in removing a section of the wall of a possibly cancerous stomach and then leaving the patient with a fistula. No diagnosis is worth such a price. There are also two technical limitations of this diagnostic method which should be fully admitted. It may be impossible for the surgeon to select for such examination the essential part of the tumor. There are instances in which dozens of sections have been made through inflammatory or other non-malignant tissue before the cancer was revealed. Again, some tumors are of such a nature that a correct diagnosis cannot be made by a few minutes' study of hastily prepared sections. Admitting all these limitations the method is of much real value, and is often of the greatest aid to the patient or his friends in deciding upon a radical operation.

Operation for cancer which is beyond the probability of radical removal is a subject worthy of more careful study than it has yet received. For practical purposes the special reasons for operation suggested under classes three and four are grouped together, for the social reasons for operation, no matter how urgent they may be, are almost always dependent upon some distressing physical condition; so in order to meet the social requirements the operation must be planned to relieve the physical distress.

But what is the usual procedure when a patient comes with an advanced primary growth, or with a recurrence, and asks for help? The surgeon, according to his temperament, gives a rosy prognosis or a guarded one. At all events he promises to do what he can. Now what he does is usually to follow the technique of a radical operation, just as far as he thinks the patient's recuperative power will permit, and then closes the wound as best he may; perhaps saying to himself or to an assistant, "Well, I got the most of that out."

This whole conception of operation under such circumstances is wrong. One should rather analyze the case and adapt his pro-

cedure to meet the difficulties which are present. There is the patient's dread of his disease and the fear that it cannot be removed by operation. Any operation well performed, with suitable mental suggestion, will allay this fear for a time; but few patients are today so uneducated or so simple as to give up all their fear at the command of the surgeon. Only returning strength for a long period after an operation will give them full confidence. All the patients in the class we are now considering are doomed to disappointment within a year or so in respect to a complete cure. Hence a prompt recovery from operation and good health for as long a period as possible are the chief aims of the operation—not the removal of extensive fascial planes, which at a late date may become cancerous, provided the patient lives long enough.

One cannot hope to formulate specific rules to cover the wide variety of conditions which cases of advanced cancer present to the operator, but there are certain general principles which ought certainly to be regarded.

1. The removal of the visible growth is desirable so far as this can be accomplished without sacrificing important muscles, nerves, etc. Although one need not feel obliged to remove so wide a margin of sound tissue as is the rule in the radical operation the natural limits of the growth should be removed with it whenever possible. For example, if it is attached to periosteum the periosteum should be removed too. If it infiltrates a muscle at least the affected part of that muscle should be removed. To cut through a cancerous nodule or gland and leave a half or a third of it behind is most unfortunate, and yet the limitations of this type of operation sometimes compel one to do this very thing.

2. The wound should be so shaped that it can be entirely closed. Skin grafts or a granulating wound are allowable in a radical operation, whereas a partial operation, which leaves a patient with a cancerous ulcer which did not previously exist, must usually be accounted a failure. If drainage is required it should be such that there will be no permanent sinus whenever this can possibly be accomplished.

3. Lymph glands should be removed if they are readily accessible, even if deeper ones which are known to be involved are left behind. Thus in some cases of carcinoma of the breast, with axillary glands involved in chains running up to the points where the vessels perforate the chest, the patient derives more benefit from a moderate clearing out of the axilla with preservation of at least a part of the pectoral muscles, and plenty of skin to close the wound, than she does from an extensive operation, with its higher mortality, longer convalescence, and limited usefulness of the arm. Why not let such a patient get up in five days, leave off bandages in ten days, and enjoy good health for a year or perhaps more, than to squander her potentials of happiness in an

effort to reach the unattainable? Let us adapt the operation to the conditions of the patient, or, in other words, to keep in mind while operating the true value of the operation for that particular individual.

4. It is of the utmost importance to save the patient's vitality by making the operation short, keeping the body warm, using a minimum of anesthetic, and above everything else, by keeping the loss of blood down to the smallest possible point. Such a patient's blood is his capital, which if lost he can replace only in a slight degree. The operator who squanders this blood capital therefore does him an irreparable injury. The careful operator will so perform his work that in most cases within a few days the patient will be able to enter into such enjoyment of life as conditions permit. An operation which entails a convalescence extending over weeks or months may be worth while if it promises even a chance of life prolonged for many years. If a patient has at the best only six months or a year of comfort before him it is obviously bad management to compel him to devote a quarter of that time to recovering from an operative shock, especially when there is the added fact to be reckoned with that the limit of his power to recover is easily exceeded.

5. If operation is performed for a special object, such as the relief of a plastic defect or to reduce the size of the mouth so that the saliva will not escape or to close a sinus in the cheek or to lessen the blood supply of the cancer, it is generally wise to limit the operation to its particular object, resisting the temptation to excise a few portions of the tumor because they are easily reached. Such excisions, unless they are so made as to include the growing edge of that part of the tumor, are often worse than useless, as they waste the patient's blood and do not prevent recurrence for a period long enough to repay him.

6. Plastic operations involving skin which is actually in contact with a cancerous growth may be successfully performed, and in case of slowly growing tumors they are often well worth while. There are instances in which such patchwork frequently repeated has kept a patient comfortable and more or less presentable for years after the possibility of any radical removal was exhausted.

7. Curettage or scraping of an ulcerating cancer is of doubtful efficacy. Sometimes it may be of use in checking hemorrhage, but usually it causes a positive blood loss at the time of its performance which can ill be spared. Its bad results are more noticeable in the case of rapidly growing tumors, in which it may fail to give the patient even temporary relief.

In order to estimate the true value of operation for cancer we must know first the object of the operation and next its result. This brings us to the second part of our subject. In looking over the published reports of work in this field we are again struck with

the fact that the possibility or failure of a radical cure dominates the surgical mind both in performance of operation and consideration of results. One may readily admit that duration of life following operation and freedom from recurrence are indeed the two great important facts which can be readily tabulated, and about which there can be little difference of opinion. But to the patient, improved function and improved appearance are equally important facts, although very difficult to tabulate or record accurately. The Scotch have a saying that "No man should thin his own turnips." Truth would be the gainer if no man estimated his own operative results, and yet in most cases no one else can do so.

In the records of these cases every endeavor has been made to minimize subjective opinion and to give the exact facts. The condition of all of the patients has been noted at the end of six months to make comparisons the more easy. All patients operated upon by the writer or his house surgeon in hospital and private practice, for real or suspected malignant disease, between April and October 1912, have been included in the list. The difficulty of keeping in touch with hospital patients is well known. By making almost monthly inquiry all of these, with few exceptions, have been followed.

It would take too much space to give abstracts of these individual records, so they have been grouped, and the results in the various groups will be noted.

Operations of the Radical Type. In the first group are included all operations in which the local growth, whether primary or recurrent, was apparently entirely removed. In a few cases the usual radical operation was somewhat modified, because of the strong probability that metastases existed beyond the operator's reach. Such patients undoubtedly have recurrences awaiting them even though they may not show for months. These are the patients for whom one wishes to obtain a quick recovery from operation by moderating the severity of the extreme radical type.

There are 27 operations in this radical group performed upon 25 patients, 2 of the patients having tumors on different parts of the body. There was no mortality from these operations.

There were 10 operations for epithelioma of the skin in various parts; 4 for epithelioma of the lower lip; 2 for epithelioma of the mouth; 6 for carcinoma of the breast; 1 for carcinoma of the uterus; 3 for sarcoma of the mouth; 1 for a recurrent sarcoma of the shoulder.

The condition of these patients at the end of six months as nearly as could be ascertained is as follows:

Examined and found without evidence of disease, 14; reported by letter to be free from disease, 3; have possible recurrence, 2; have certain recurrence, 1; died from recurrence, 2; passed from observation, 3; total number of patients, 25.

Operations for Diagnosis. In the second group are placed 6 operations performed for diagnostic purposes in conditions of doubtful malignancy, although 4 of the patients had had previous operations. One patient had been twice operated on in other hospitals for cancer of the mouth. The removal of necrotic bone was followed by subsidence of symptoms, the condition probably being inflammatory. One patient came with recurrent ulcers of the forehead, which were excised and successfully skin-grafted. They were probably tuberculous. One patient had a swelling of the right hip nine years after removal of the right kidney for sarcoma. A lymph gland was removed and found normal. Tissue previously removed in another hospital by a deep incision into the hip had also been found to be normal. Examination with the *x*-rays was negative, yet malignancy must have existed, for the patient's pain and emaciation continued, and she died in about four months. The fourth patient had a leukoplakia of the tongue, a section of which was found to be merely papilloma. The fifth patient had a painful swelling of the posterior part of the lower jaw, variously diagnosticated, and which was operated on three times before the swelling and pain and discharge disappeared. It was possibly an aberrant wisdom tooth. The sixth patient, married, aged thirty-six years, had a painless, fluctuating tumor of the breast for ten months. It was about one and one-half inches in diameter and contained purulent fluid. A section of its wall showed it to be inflammatory. All of these patients recovered promptly from the slight operations, the wounds of the second, third, and fourth healing primarily, and those of the others by granulation.

Their condition at the end of six months was as follows:

Well, no sign of cancer, 2; well, after another operation which failed to reveal cancer, 2; died, probably from undiscovered cancer, 1; passed from observation, 1; total, 6 cases.

Operations for Special Objects. In the third group are included the operations performed for some special object upon patients whose apparent tumor or tumors could not be entirely removed. While the social and physical reasons for operation should both be considered in deciding for or against an operation, and in determining the nature of such operation, they so often coexist that it is quite impractical to separate these patients into two classes.

There was no operative mortality among the 24 patients of this group, as there ought not to be. One is justified perhaps in taking extreme risks in the attempt to accomplish a radical cure. There is not much excuse for sacrificing a patient's life in the attempt to give him temporary relief. While making all allowance for unknown weakness of a patient's organs, and unforeseen accidents during operation, it is still true that the operative mortality in this type of operating can be kept near the zero mark if the

surgeon carefully estimates the patient's power of resistance before operation and adheres to his resolve not to go beyond this point.

Ten of these patients had growths situated in or connected with the mouth. Only one of these was primary, the others were local recurrences, following one, two, or three operations. The object of operation in these cases was the removal of a painful or ulcerating tumor or to close a defect in the mouth. The periods of time through which such ends were accomplished and maintained, if expressed in months, would be 0, 1.5, 2, 2, 3, 4, 4, 5, 6, an average of not quite three months of comfort per patient. This is not the duration of life, but the period during which the patient could fairly be said to be in a distinctly better condition locally than before the operation. Five of the 10 patients died; 1 at two months from a more extensive operation performed elsewhere; 2 from recurrence in three months; and 2 from recurrence in four months. The remaining 5 were living at the end of six months, but, as stated above, only 1 of them was in a better condition than before his operation.

In 3 cases a recurrent tumor was situated in the antrum and orbit. One of these patients was in good condition for about four months. Then his pain recurred, and at the end of five months he was operated upon by another surgeon and died in three days. The other 2 patients received little or no benefit from operation, and both died in six weeks from extension of the disease.

In 2 cases recurrent tumors were situated in the neck and were very extensive. There was a partial removal in 1 case and an arterial ligation in the other. The first patient received very little benefit and died from an extension of the growth in less than two months. In the other case the deeper part of the growth seemed checked, but the superficial ulceration continued until it reached from ear to ear across the front of the neck. The patient was in good general health at the end of four months, but on account of the ulceration it is only fair to credit the operation with two months of improvement.

A recurrent epithelioma of the scalp, involving the skull, was widely excised, with the periosteum under the whole area of diseased scalp and a smaller portion of the skull. The wound granulated well, but the patient's headaches were not entirely relieved. In four months an additional amount of skull was removed, together with the dura mater, which the growth had penetrated. The patient again recovered promptly from operation, but headaches continued. He gained in health for a short time and then began to lose. At the end of six months he was somewhat anemic and had an almost constant pain. Three months of improvement is as much as can be credited to his first operation.

In one case of mixed-celled sarcoma in the parotid region, recur-

rent after two operations, a great mass of tumor tissue was removed, but it was found impossible to remove the growing edge of the tumor anywhere in the deeper portion. Consequently a rapid recurrence took place, so that although the wound healed primarily, local improvement could scarcely be said to have exceeded one month. The later history of this patient is unknown.

In 2 cases a painful recurrent breast tumor was removed from the wall of the chest and the wound covered with a flap of skin, taken in 1 case from the opposite breast. The wounds healed primarily, and the patients were in better local condition than before the operation, for periods of two months and four months respectively.

An extensive carcinoma of the vulva and groin was excised. Glandular involvement had already extended to the retroperitoneal and iliac and lumbar glands at the time of operation. Both wounds healed promptly, and although the external appearance was good for two months, pain and anemia progressed with scarcely any interruption, and the patient died in four months, with practically no benefit from operation.

A man with recurrent epithelioma of the perineum which extended into the deeper part of the pelvis beyond the ischium, too far for its safe removal, healed primarily and left the hospital entirely free from pain. In three months it was necessary to repeat the operation on account of a fresh recurrence, and this time the relief was of shorter duration. The patient wrote at the end of six months that at times he was suffering intensely. Two months is a fair estimate of the period of improvement attributable to the first operation in this case.

Two patients with extensive carcinoma of the uterus were treated by ligation of the internal iliac arteries. These patients had not been operated upon previously. In each case the abdominal wound healed primarily, and there was less hemorrhage and discharge than before the operation. Pain and emaciation continued in one case to such an extent that the operation had little more than a social value, although the patient was still able to get about at the end of six months. The other patient has been lost sight of.

One patient with extensive abdominal carcinoma was operated upon to satisfy the family. The growth was so widely disseminated that nothing could be removed. This patient died suddenly in about three weeks, possibly from embolism. There was no improvement from this operation.

The summary of these operations for special objects performed upon 24 patients shows:

Mortality from operation, 0; average period of improved health attributable to operation, two months; number of patients living at six months, 11; number of patients dying in less than six months, 11; number of patients lost sight of, 2.

An average gain of two months of improved health, may seem to some hardly worth striving for, but this is rarely the attitude of the patients. They are not only most grateful for any relief, but many of them take great pride in even temporary victory in a fight in which they know they must ultimately lose.

In conclusion it may be said that not every patient with a recurrence should be operated upon. There should be some special object to be obtained by such operation. The operation should be shaped to meet such special object, and should not be patterned after the radical operation. All patients who have been operated upon for cancer should be followed month by month, and single recurrences favorably situated should be promptly removed.

THERAPEUTIC ARTIFICIAL PNEUMOTHORAX.[1]

By Herbert Maxon King, M.D.,

PHYSICIAN IN CHIEF,

AND

Charles Wilson Mills, M.D.,

ASSOCIATE PHYSICIAN TO THE LOOMIS SANATORIUM, LIBERTY, NEW YORK.

The employment of pneumothorax, artificially induced, for therapeutic purposes was attempted at Loomis Sanatorium first in 1898, following the plan devised by Murphy. But few cases were so treated, however, and as the results were not such as to encourage a continuance of the method it was promptly abandoned. More recently the published reports of the satisfactory results attained by Forlanini, Brauer, Spengler, Saugman, and others in Europe, and Robinson and Floyd in this country, threw a much more encouraging light upon the procedure, and induced us to consider its readoption as a remedial measure in certain selected cases.

The beneficial effects of immobilization of an actively diseased lung as the result of a serous effusion into the pleura have long been recognized, and it has been our practice at Loomis Sanatorium not to aspirate in such cases unless pressure symptoms compelled us to do so, and then only to such an extent as would relieve the embarrassment, and to regard with satisfaction the occurrence of hydrothorax whenever it appeared on the affected side in the presence of an active and progressive lesion.

When it became apparent therefore that by means of an improved technique immobilization and compression of the diseased lung

[1] Presented in abstract at the Mid-winter Meeting of the American Sanatorium Association at the Montefiore Sanatorium, Bedford Hills, New York, December 7, 1912.

could be effected without serious danger to the patient, and with some promise of symptomatic relief, or even permanent benefit, in advanced and progressive cases, we determined to employ the procedure, but, for the time at least, to limit its employment to this unfortunate class and not to attempt it until the more conservative measures had failed. So far we have adhered to this practice, and have limited the treatment to such cases only as presented evidence of progressive disease in one lung and a comparatively slight lesion in the other, and where the prognosis has been unfavorable. This principle has governed our selection of cases for treatment at Loomis Sanatorium. For that matter, however, our rules for the selection of suitable cases are those generally followed.

A few enthusiastic advocates of the method have advised the procedure in early favorable cases, and have reported excellent results in such cases. But as the prognosis in this class is favorable for arrest under the ordinary dietetic hygienic treatment, the additional advantages of an artificially induced pneumothorax are questionable. The procedure is a radical one in any case, and while it is justifiable in those who have progressed unfavorably despite treatment by the ordinary methods, and in whom the prognosis is undoubtedly bad, we have felt that in the present state of our knowledge it should be limited to this class.

Selection of Cases. Forlanini considers the following as indications for treatment by induced pneumothorax:

1. Uncomplicated unilateral phthisis, with slow or subacute course, and with a pleura free from adhesions, regardless of the degree of the lesion.

2. The same with such adhesions as may be removed by artificial pneumothorax.

3. Bilateral phthisis not running an acute course and with lesions on both sides not far advanced.

Claude Lillingston regards as favorable for treatment:

1. Cases of extensive and acute disease of one lung coupled with slight or no disease of the other lung.

2. Certain cases failing to respond to ordinary methods even with considerable disease of the better lung.[2]

Herbert Rhodes[3] advocates the treatment in cases of

1. Pulmonary tuberculosis limited almost if not entirely to one lung.

2. Recurrent hemoptyses if at all severe.

3. Continued fever, cough, and general increase of disease on one side while the other lung is healing or only slightly affected.

Volhard,[4] admitting that the first essential is the absence of large adhesions in the pleura, states that only an actual trial is

[2] Lancet, July 15, 1911.

[3] British Med. Jour., October 28, 1911.

[4] Munch. med. Woch., August 6, 1912.

capable of establishing the presence of such adhesions, and that physical signs and *x*-rays are of little value in determining this point. He considers that, so far as possible, the disease should be confined to one side though it may embrace the entire lung. The most suitable cases are those of unilateral cavities. Cases of "caseous pneumonia" are questionable. Severe hemoptyses may often be controlled. Abscess of the lung and miliary tuberculosis are not suitable. (Our experience in Case XII bears out this view with regard to abscess.) Severe cases of bronchiectasis are suitable, but require long continuance of treatment.

Klemperer[5] in a paper on the subject advocates artificial pneumothorax in every case with continuous fever and much expectoration, when the condition is not too desperate, although he naturally considers unilateral cases most favorable. He does not advocate the procedure in early and otherwise favorable cases.

Almost all writers on the subject agree that slight or moderate laryngeal complications not only do not contraindicate the treatment, but are usually markedly benefited thereby, and a few report good results in tuberculous complications of the intestinal tract.

Robinson and Floyd,[6] regard as most suitable for compression therapy such cases as present unilateral disease, but do not consider as contra-indications slight and comparatively inactive lesions on the opposite side.

With regard to first-stage cases, these authors argue—with what seems to us excellent judgment—that because in such cases pneumothorax *can* be readily established it is by no means proof that it *should* be, and that there is no reason to believe that pneumothorax therapy should be substituted when suitable institution or home treatment can be conducted.

Among the 102 cases reported by Brauer and Spengler[7] many of the good results occurred in bilateral cases.

Paradoxical as it appears, notwithstanding the increased mobilization of the untreated lung improvement in the lesion on that side seems often to occur simultaneously with the improvement in the other lung, which is being treated by immobilization, although this does not always follow, as evidenced in Case VII of our series.

The most plausible explanation of this fact and that most generally accepted is that the improved condition and heightened resistance resulting from the reduced toxemia after successful compression place the patient in a much better condition for coping with the situation in the untreated lung.

In our series all of the tuberculous cases have been "far advanced" and bilateral, but in almost every instance the disease has been slight and comparatively inactive on the untreated side.

[5] Berl. klin. Woch., December 18, 1911.
[6] Arch. Int. Med., April 15, 1912.
[7] Beitr. z. Klin. d. Tuberk., 1911, xxx.

TECHNIQUE AND APPARATUS. In none of our cases have we employed the open method of Brauer, although we realize that under certain conditions this method might be safer and more expedient, especially with beginners. But as we have so far met with no serious mishaps with the Forlanini puncture method, and as it is much easier to gain the patient's consent to this procedure, our experience is limited to this method.

When we decided to reintroduce artificial pneumothorax at Loomis Sanatorium we asked Doctor Cleaveland Floyd to come and demonstrate the technique and apparatus employed by Doctor Samuel Robinson and himself in their work.[8] To this Doctor Floyd kindly consented, and the first injections were made by him in July, 1911. Five patients were selected as apparently suitable cases (Cases I, III, IV, XI, and XIII of our series). He brought with him the apparatus devised by Robinson, and Floyd needles, which he has modified from those used by Brauer, together with sufficient nitrogen for the first injections. Subsequently, and for several months until we were able to obtain a Robinson apparatus and the Floyd needles, we improvised a home-made apparatus with common aspirating needles, which answered the purpose, and as we were unable to obtain nitrogen at that time we used atmospheric air with apparently satisfactory results, except for the necessity of more frequent injections. From the start we have used a water manometer, which is very delicate and quite satisfactory except in cases with decided negative pressure, when it is sometimes awkward by reason of its delicacy.

Spengler employs a double manometer—one with a water column and the other with a mercury column, the latter to be used in cases with more pronounced negative pressure. This arrangement is obviously very convenient and time-saving.

In the selection of a site for the initial puncture we have been governed entirely by physical signs, avoiding proximity to cavity areas, as indicated by auscultation, and endeavoring to select a point where resonance on percussion and auscultatory signs indicate some respiratory activity and freedom from adhesions. In the main we have kept to the anterior and posterior axillary lines, but occasionally have made injection through the anterior chest wall as high as the fourth interspace and posteriorly to the angle of the scapula. The choice of site has been governed by convenience in each case. This settled the patient is given a hypodermic injection of morphine, $\frac{1}{16}$ to $\frac{1}{8}$ grain, and presently is placed upon the side opposite to that which is to be injected, with a pillow beneath to effect the greater separation of the ribs. The area selected for the puncture is painted with tincture of iodine. The parts are then

[8] For description of this apparatus, see articles by Robinson and Floyd in Trans. Amer. Clim. Assoc., 1911, and Arch. Inter. Med., April 15, 1912.

anesthetized with a 1 per cent. solution of novocaine injected slowly—at first beneath the skin, then deeper, and finally a small amount into the pleural sac, when by the sensation of suddenly released resistance the point of the needle is believed to have passed the parietal pleura. It is seldom necessary to freeze the surface with ethyl-chloride, and patients very seldom complain of pain as the result of the introduction of the needle if a few minutes are allowed after the novocaine injection before proceeding.

We have customarily made a small incision through the skin with a sharp scalpel before introducing the pneumothorax needle, to avoid the pressure otherwise necessary to force the point of the large needle through the skin. The latter, with the stylet in place and the branch connecting with the manometer and nitrogen reservoir shut off by the valve-cock, is now introduced, preferably at a slight angle to avoid injuring the visceral pleura. The same sense of release of resistance, but more marked, that one notices in the preliminary injection of novocaine, generally indicates the puncture of the parietal pleura. The stylet is then withdrawn and the valve of the stylet tube closed. The branch valve is then cautiously opened and the movements in the water or mercury column in the manometer observed. The valve in the tube connecting with the nitrogen reservoir is, of course, closed. If the point of the needle in the pleural sac is not plugged and there are no extensive adhesions at this point, the manometer will indicate a more or less pronounced negative pressure with oscillations corresponding to the respiratory movements.

In the presence of extensive adhesions there will be little or no negative pressure or oscillations, while if the point of the needle has pierced the lung and is in communication with a bronchus there will be no sustained negative pressure, but oscillations may be quite as pronounced as when the point of the needle is in the pleura. Oscillations alone, therefore, do not necessarily indicate that one is between the pleural layers (see Case III).

F. Pielsticker and H. Vogt[9] state that holding the breath by the patient readily shows on the manometer whether we are in the pleural sac or not. This does not appear to us to be a fact, however, for if the point of the needle is in communication with a bronchus and the patient holds his breath with the glottis closed a positive manometer reading may be registered just as it may when the point of the needle is between the pleural layers. In short, we have felt that a more or less pronounced negative pressure, with respiratory oscillations, are the only safe indications for the introduction of the gas.

When these indications are met we may safely assume that we are in the pleural sac. The manometer valve is then closed and the

[9] Monatsschrift f. Kinderheilkunde, Leipsic.

gas allowed to pass into the chest. In the presence of a pronounced negative pressure this should be controlled by the valve, and permitted to run but slowly to avoid the shock of too rapid collapse of the lung.

The amount of nitrogen which may be safely injected at the initial puncture must, of course, depend upon the conditions in each case, but even when a negative pressure persists and no other contra-indications present, it is probably safer to limit the first injection to a few hundred cubic centimeters. Robinson and Floyd give as a maximum for the first injection 1000 c.c.

Bonniger[10] believes that in a strong man 2000 c.c. and in a woman 1600 c.c. may be given at the first injection if manometer readings do not contraindicate. This seems to us unnecessarily heroic and not altogether devoid of embarrassing sequelæ if not of danger.

It is desirable, however, if possible to induce at the start a sufficient pneumothorax to give some symptomatic relief, either in lessened cough and expectoration or reduced fever, if for no other reason to encourage the patient more cheerfully to coöperate in subsequent treatment. But this can usually be accomplished by 500 c.c. or 600 c.c., and such an amount rarely gives any sense of discomfort to the patient. In most cases, without extensive adhesions limiting the amount of the initial injection to this figure, there will still be a negative pressure at the end of the injection.

Subsequent injections had best be made at intervals of not more than a few days until the manometer readings are neutral or slightly positive, and the *x*-rays show as complete a lung compression as is possible. After this is accomplished the intervals between the injections are governed by symptoms—especially the amount and character of the sputum, temperature, etc., and the *x*-rays. If atmospheric air is used the intervals will necessarily be shorter than when nitrogen is employed.

More or less effusion occurs in about one-third of the published cases, and according to some of the German writers has an inhibitory influence upon the gas absorption. This has seemed to be a fact in our experience.

The amount of gas injected after the initial operation is determined by the manometer readings and the feelings and condition of the patient. We have thought it neither necessary nor advisable to secure a marked positive intrathoracic pressure, and have been content with a neutral or very slightly positive manometer reading at the conclusion of the injection. Even this sometimes gives a sense of "tightness" and slight temporary discomfort, especially during the early stages of treatment.

The manometer is the key to the whole situation, and is the one device which has made artificial pneumothorax practicable as a

[10] Berl. klin. Woch., August 26, 1912.

therapeutic measure. The other accessories to the operation are more or less a matter of convenience. One may improvise an apparatus using a plain trocar or aspirating needle, and employ atmospheric air in place of nitrogen if necessity or expediency compel, but a manometer is an essential to the success of the treatment.

The accidents which may occur in the process of inducing pneumothorax are fully described in the literature. The principal ones are pleural reflex, gas embolism, and surgical emphysema. With care and a little experience in the method they are for the most part avoidable, but when they do occur they are somewhat disconcerting.

In our experience we have met a mild "pleural reflex," pleural "eclampsia" (Forlanini) once (Case IV). Robinson and Floyd believe that novocaine anesthesia of the pleural membranes obviates the risk of this complication, and Rhodes states that if the nitrogen is warmed "pleural reflex" is impossible. In our case novocaine was not employed and the atmospheric air which we were using at the time was not warmed. It is possible therefore that one or both omissions were responsible.

It does not seem to us that air embolism is a serious menace if reasonable care is exercised and the behavior of the manometer is understood and closely watched. In our early experience, when on one occasion we injected air into the lung, which escaped through a bronchus (Case III), we made the mistake of relying upon the manometer oscillations in the absence of negative pressure, but had our needle point been in a bloodvessel there would have been no oscillations and we should not have proceeded.

We have met with a mild and unimportant surgical emphysema about the point of puncture several times, with little or no consequent inconvenience. A more serious matter was that of Case X, when by reason of adhesions the nitrogen made its escape along the trachea and into the subcutaneous tissue of the face, neck, and chest on the side opposite to that injected, causing for a time a disconcerting dyspnea through involvement of the submucous tissue in the larynx.

In the 16 cases here reported we have included 6 which proved inoperable by reason of adhesions. For statistical purposes these should be excluded, but we have included them because they have seemed to us in some respects instructive. We have classified our cases on a basis of results attained, and they are not arranged in sequence as to point of time.

Of the 10 operable cases, as is shown in the summary, 2 have shown marked and apparently permanent improvement; 7 have shown temporary improvement and more or less symptomatic relief, while in 1 case of lung abscess no improvement was observable. As has been stated our cases have all been far advanced,

active, and bilateral, with decidedly unfavorable prognoses, a fact which should be borne in mind when considering the results attained.

Since October, 1912, we have been controlling the injections by means of the *x*-rays. Some of these plates are reproduced.

We look upon the method with more confidence as we proceed and in our later cases—too recently placed under treatment to justify report at this time—we feel encouraged to hope for better results than it is possible to report in the present series. In any case there is no small satisfaction in the consciousness that we possess a means by which we can offer another chance of life, slender though it may be, to this forlorn class of otherwise hopeless invalids.

CASE I.—J. P. C., male, aged twenty-two years. Admitted April 15, 1911. Condition: far advanced. Turban iii (R iii–L i). Duration of disease: since September, 1910 (ten months).

Symptoms. Since admission in April has had persistent hectic fever (98° to 99° in A.M., 101° to 104° in P.M. Pulse, 100 to 120. No normal days since admission).[11] Cough: expectoration averaged from 140 to 190 grams per day. Continued loss of weight; 4.15 kg. since admission. Patient on absolute rest in bed.

Physical Signs. Extensive involvement of whole right lung, with excavation of most of the upper lobe. Slight infiltration scattered throughout left lung, mostly at root. On account of extensive rapidly progressing destructive lesions and of severe constitutional disturbance this case was regarded as almost hopeless—in fact, practically moribund.

July 30. First injection of 750 c.c. of nitrogen without difficulty. Evidently slight if any adhesions. Marked immediate improvement; temperature falling to normal on the following day and remaining there subsequently. Expectoration dropped from 160 on the day of operation to 65 grams on two succeeding days, then rose again to from 120 to 160 grams.

August 8 to September 14. Three injections of air, each of about 1000 c.c. Marked continued improvement.

October 15. Signs of fluid have replaced pneumothorax signs in right chest. Injections therefore discontinued.

January 18, 1913. Up to the present date patient has made steady improvement. He is now walking three or four hours a day, and his weight has increased from 42.75 kg. at time of first injection to 63.52 kg., a gain of 20.77 kg. (45 pounds). The expectoration still remains rather high, averaging about 90 grams a day. Tubercle bacilli have been very few since establishment of pneumothorax, never more than No. V (Gaffky scale), and sputum examinations sometimes have been negative for several months in succession.

[11] In this article all temperatures are recorded from rectal observations.

Physical examination and *x*-ray plate indicate a markedly fibroid contracted right lung with pleural thickening, and a resultant retraction of chest walls, diaphragm, and heart. Left side clear (see Fig. 1).

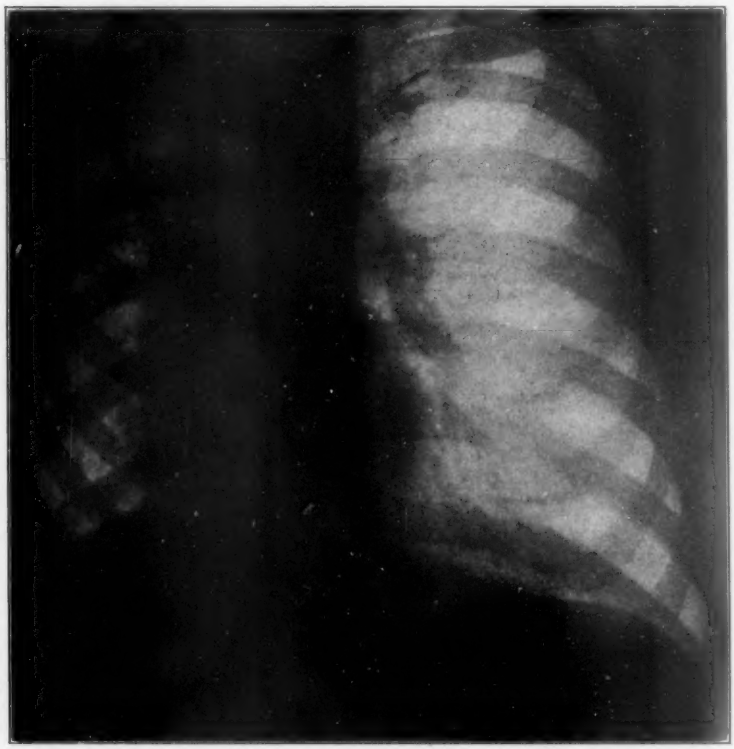

FIG. 1.—Case I. November 23, 1912. Shows marked contraction of right lung with resulting contraction of chest walls, diaphragm, and heart. Densely infiltrated upper lobe. Slight infiltration at left apex and root.

Summary. Satisfactory result in a progressive and seemingly hopeless case, the beginning of improvement following immediately on injection of pleural cavity.

CASE II.—A. A. N., male, aged nineteen years. Admitted September 5, 1912. Condition: far advanced. Turban iii (R iii–L i). Duration: since spring of 1912.

Symptoms. Periods of slight fever, expectoration averaging 50 grams a day. At rest in bed.

Physical Signs. Indicate active infiltration throughout most of right lung; most marked in upper lobe. Slight inactive infiltration in left upper lobe.

October 16. First injection of 800 c.c. nitrogen without difficulty. Pressure still negative at end. Temperature, which had been 100° or slightly over every afternoon, on second day after operation became normal and remained there.

October 22. 700 c.c. injected. Continued normal temperature; expectoration falling steadily. Patient was started on five minutes' walking, twice a day, gradually increased.

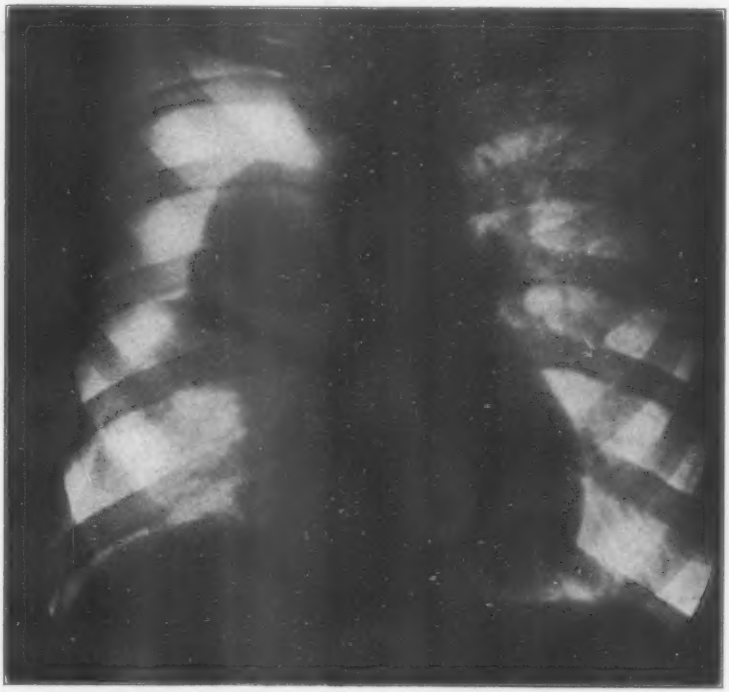

FIG. 2.—Case II. November 12, 1912. Shows pneumothorax occupying right chest, upper lobe of lung collapsed, middle and lower lobes partially collapsed. Probable diaphragmatic adhesions preventing complete collapse of lower lobe.

January 18. Injections have been continued until present at intervals of one to three weeks, from 500 c.c. to 700 c.c. each time. Improvement has continued uninterrupted. Patient is on manual labor squad, working three or four hours a day. Expectoration only 2 to 4 grams a day. Continued weight gain (see Fig. 2).

Summary. Very satisfactory result. Arrest of activity and continued improvement following institution of pneumothorax.

CASE III.—J. H. D., male, aged forty-four years. Admitted June 6, 1911. Condition: far advanced. Turban iii (R iii–L i). Duration of disease: since 1901 (ten years).

Symptoms. Remittent fever, 99° to 101° most of the time since admission. Pulse, 68 to 90. Cough; expectoration averaging 172 grams in June and 128 grams in July, the month previous to first injection. Patient at rest in bed.

Physical Signs. Indicate extensive long-standing involvement of the right lung, with probable cavity in the upper lobe; much less marked infiltration in the upper lobe of the left lung.

Complication. Slight grade of nephritis, without enlargement of heart. Rather persistent extrasystole of heart beat, occurring usually about every six beats.

July 30. First injection of 700 c.c. of nitrogen in the right pleural sac. Apparently no adhesions. Following the injection sputum weight fell slightly for a few days, from 145 to 106 grams., then rose to 150 grams again. No change in fever.

August 8 to September 2. Four injections of air from 1000 to 2000 c.c. each made. Some improvement in condition shown by normal temperature and lower sputum weight (70 grams per day).

September 19. An attempt was made at injection, in several places, but impossible to get manometer reading showing needle in pleural sac. Needle probably entered lung, as on the following day there was about a dram of blood in sputum. Physical examination showed dulness in the lower part of the right chest, with very deficient breath sounds. Expectoration, however, remained at comparatively low figure, and exercise was gradually increased to thirty minutes, twice a day. Had also gained about 4.5 kg. of weight.

October 27. Another attempt was made at injection. Oscillations obtained on manometer, but no negative pressure. Needle was supposedly in pleural sac, and 2000 c.c. of air were injected. No change in manometer reading, and no evidence from physical signs of any resulting pneumothorax. Therefore conclusion was reached that the point of the needle must have passed through the adherent pleura into the lung, and that injected air passed out through the bronchi. Further attempts at injection were abandoned.

Patient's condition continued about the same until February, 1912, when severe hemoptysis occurred. After this his condition became gradually worse until discharged from the Sanatorium, May 24.

Summary. Temporary improvement followed injections. This case illustrates the danger of allowing too long a time to intervene between injections, unless condition of compression of lung is carefully controlled by physical examination or better by *x*-ray plates. Undoubtedly between the injections of September 2 and the attempt at injection on September 19, an interval of seventeen days, the air had become absorbed and the pleural surfaces adherent.

This case illustrates also the inadvisability of proceeding with

the injections in the absence of negative pressure, as shown by the manometer even in the presence of characteristic oscillations.

CASE IV.—M. J. T., male, aged thirty-two years. Admitted November 6, 1910. Condition: far advanced. Turban iii (R iii –L i). Duration of disease: since 1906 (five years). Chest examination indicates: Right, extensive infiltration throughout lung, with excavation in upper lobe. Left, compensatory changes, with probably small areas of infiltration, principally at root.

Symptoms. Fever, remittent (98° to 101°); cough; expectoration averaging over 100 grams a day. Patient at rest in bed.

Complication. Toxic nephritis.

July 30, 1911. First injection of 750 c.c. nitrogen into right chest. Following this there was no special change noted in symptoms, except slight decrease in expectoration.

August 8. 650 c.c. of air. Patient very nervous during operation, and in condition verging on collapse immediately following. Results of this injection appeared to be a further slight decrease in expectoration and a lower temperature range.

August 16. 400 c.c. of air. Severe collapse following operation, with rapid feeble pulse and loss of consciousness ("pleural reflex"). For this reason further injections were discontinued.

August 25, nine days after operation, temperature became lower and remained practically normal except for occasional days (never reaching, however, 101°). Expectoration also less for several days after injection, running from 60 to 120 grams, but amount gradually increasing after discontinuance of injections.

September 15. Severe hemoptysis, followed by death.

Summary. Slight temporary improvement in condition following injections. Probably a case of "pleural reflex."

CASE V.—I. J. A., female, aged twenty-four years. Admitted September 21, 1910. Condition: far advanced. Turban iii (R iii–L ii). Duration of disease: since March, 1910.

Symptoms. Almost constant daily remittent fever during the year following admission. Temperature usually between 101° and 102° in the afternoon. Night sweats. Loss of weight, 10 kg. (22 pounds) since admission. Expectoration averaging between 150 and 200 grams daily. In bed or sometimes sitting up in a chair for a few hours, since admission, except for a few days in December, 1910, when, during a period of temporary improvement, temperature was normal and she was allowed ten minutes walk, twice a day. No normal days since that time.

Physical Signs. The physical signs indicate extensive involvement of the right lung, with probable excavation in upper lobe. Compensatory and probably some fibroid changes in left lung.

November 13, 1911. First injection of 700 c.c. air into right pleural sac. Expectoration fell from 220 grams on day before injec-

tion to 105 grams on following day, remaining low for several days. No marked effect on fever.

November 16 to December 22. Eight injections of from 600 c.c. to 900 c.c. each, given at intervals of from three to seven days. Temperature now normal, and expectoration only 80 to 100 grams a day.

March 6. Injections continued at intervals of one to two weeks up to this time, condition remaining about the same, except for some tendency to increase of expectoration. Following the injection on this date the temperature gradually rose and fever was present, usually about 102° in the afternoon for the following month. Expectoration averaged about 150 grams. For a few days in the early part of April temperature was normal, but then rose again, and fever remained until discharged from the Sanatorium on May 4, 1912. No further injection given during this time. At time of discharge examination showed signs of pneumothorax throughout the right chest except at the apex, and slight amount of fluid at base.

Summary. This case was distinctly disappointing in results. A practically unilateral case, with high expectoration and probable cavity, it seemed to offer good indications for pneumothorax. But in spite of the fact that the latter was successfully established, and that the lung was apparently well collapsed, no permanent good results followed. Probably the temporary improvement in condition shown by reduction or absence of fever and lower expectoration may be attributed to the pneumothorax, but this improvement was only transitory. (Subsequent to discharge patient went to Saranac Lake, where pneumothorax has been maintained with apparently good results. At last report, December 1, 1912, patient had gained over twenty pounds, and has been feeling much better.)

Case VI.—F. S. M., male, aged forty-five years. Admitted January 5, 1910. Condition: far advanced. Turban iii (R iii–L i). Duration: since May, 1909.

Symptoms. Patient's condition for first nine months after admission in January, 1910, was steadily progressive. Short periods of fever, heavy expectoration, and loss of weight continued until patient, although six feet two inches in height, in October, 1910, weighed only 46.05 kg. (101 pounds). Unexpectedly and without any decided change in treatment he at this time began to improve, this improvement continuing most spectacularly until in June, 1911, he had reached a weight of 73.3 kg. (161 pounds, 60 pounds gain) and was on two hours' exercise a day. The expectoration did not decrease materially, however, during this time, remaining most of the time over 100 grams a day. In the fall of 1911, the patient began to lose ground again. At the time of the first injection, January 30, 1912, he weighed 65.5 kg. (144 pounds), was without fever, and had an expectoration of 171 grams a day.

Physical signs at the time of injection indicated an extensive involvement of right lung with probable excavation in upper lobe. Compensatory signs in left lung, with slight infiltration of upper lobe.

January 30. First injection of 400 c.c. of air. Pronounced negative pressure was obtained and marked respiratory oscillations, indicating absence of pleural adhesions.

February 1. Two days later 1000 c.c. of air was injected, the pressure still being slightly negative at the end of the injection. Patient complained of no inconvenience except a slight feeling of tightness through chest.

February 7 to March 25. Four injections of about 1000 c.c. each.

During this time the patient had gained a little weight (650 grams) and felt perhaps somewhat better, but the chief effect of the injection had been on the amount of the expectoration, which had fallen from 171 grams to 103 grams per day. The signs indicated an extensive pneumothorax throughout lower two-thirds of right chest. The signs continuing it was not thought necessary to repeat the injections until April 23 when 1300 c.c. of nitrogen was injected.

During May the expectoration fell to 65 grams, by far the lowest that it had been at any time since his admission. He was, however, losing weight again at this time.

June 14 to July 20. Three injections of 600, 950, and 1200 c.c.

During June and July, although there was a complete collapse of the lung, the condition did not improve, there being a continual loss of weight, and the expectoration rising again from 65 to 117 grams.

No further injections were made until September 7, the pneumothorax signs continuing.

September 7. Attempt made at injection, but most surprisingly it was found impossible to obtain a negative pressure or to get good respiratory excursions; 250 c.c. of nitrogen were cautiously injected, but it was deemed inadvisable to attempt more than this.

September 9. Another attempt at injection was made, with the same result. No negative pressure could be obtained, and only 100 c.c. nitrogen were injected.

No further injections have been attempted. The explanation of the failure to obtain a satisfactory negative pressure was not clear.

An examination on September 21 showed that in addition to the pneumothorax there was also a small amount of fluid in the right chest. These signs are still present (see Fig. 3).

The patient's condition is slowly growing worse. The expectoration has risen again to 151 grams, and the loss of weight has continued.

Summary. Temporary improvement. Disappointing case in that so complete a collapse did not give better and more lasting improvement.

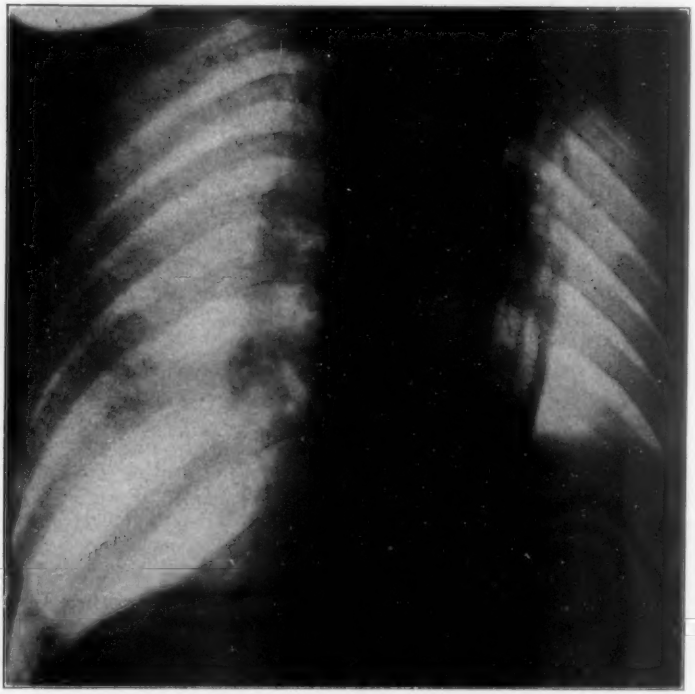

FIG. 3.—Case VI. November 12, 1912. Hydropneumothorax of right chest with collapse of right lung.

CASE VII.—J. D., male, aged forty-two years. Admitted October 1, 1911. Condition: far advanced. Turban iii. Duration of disease: since March, 1911.

Symptoms. Constant fever since admission, averaging about 98° in A.M. and 102° in P.M. Expectoration, 70 to 80 grams a day. In bed since admission.

Complications. Laryngitis of mild grade. Dry otitis media. Diabetes mellitus of mild grade. On carbohydrate restricted diet the urine had become and remained free of sugar.

Physical Signs. Indicate extensive involvement of left lung, with cavity signs in lower part of upper lobe. Slight infiltration of apex of right lung.

Case did not seem an especially favorable one for pneumothorax treatment in view of the complications and the advanced condition.

December 8. First injection of 300 c.c. air into the left chest. Temperature, which had reached 101° and over every day since admission, on the day following pneumothorax, reached only 100.4°, rising again, however, on the succeeding days.

December 12, 1911 to January 2, 1912. Four injections of from 600 to 1000 c.c. each. Marked improvement in condition. Temperature normal and expectoration less. Patient now sitting up two or three hours a day.

January 5. Graduated exercise (walking) begun and gradually increased to fifteen minutes, twice a day. This was followed, however, by a return of fever to about 101° in the afternoon.

January 17. 600 c.c. of air. Temperature again normal on following day, but immediate return of fever when exercise was resumed.

January 30. 700 c.c. of air. Temperature again fell to slightly over 100° on the following three days, although after that it rose again to 101° or over, even though no further attempts at exercise were made. Expectoration fell to an average of about 50 grams.

February 7. 700 c.c. of air. No improvement followed this injection. A few days later there was a marked exacerbation of fever, as high as 103° on most days, the expectoration rose and the general condition grew progressively worse. Although the signs of extensive disease and cavity in the left lung had at this time been replaced by the pneumothorax signs, yet on the right or "good" side there were signs of a considerable exacerbation of the disease, and this was held to be the reason for the increase of symptoms. Under these circumstances it was not deemed advisable to continue further injections. The patient's condition grew progressively worse from this time on and death occurred on May 27. The pneumothorax signs in the left chest continued until the end, although becoming much less extensive than immediately after the injections. During the last few weeks before death dyspnea was a very marked and distressing feature.

Summary. Considering the condition of the patient at the time when the injections were first made, the improvement which followed, even though only temporary, was rather remarkable. The ultimate exacerbation of the disease on the "good" side may perhaps have been due to the increased compensatory activity of that side occasioned by the pneumothorax, though there is no real evidence leading to such a conclusion aside from the old *post ergo propter* argument. Even if so it is the only case in which we have seen any exacerbation of the disease that could be attributed, even remotely, to the pneumothorax, and we feel that the contingency is so remote a one that it may be reasonably disregarded in properly selected cases.

CASE VIII.—R. F., male, aged eighteen years. Former Sanatorium patient, resident of Liberty. Condition: far advanced. Turban iii (R i–L iii). Duration of disease: since 1908 (three years).

Symptoms. Severe continued hemoptysis over period of several days. Disease rather rapidly progressing since previous summer. Temperature and pulse normal.

Physical Signs. The physical signs indicate extensive involvement of the left lung, with numerous bubbling rales. No signs of moisture on the right. Thorough examination was not made at the time of injection on account of hemoptysis.

Pneumothorax was attempted on this patient as a means of checking the hemorrhage. As the left lung had been the one chiefly affected at the time of his residence in the Sanatorium, and as a superficial examination at the time of the injection showed the evidence of abundant moisture in the left lung, it was assumed that this was the seat of the bleeding.

November 27. First injection. Puncture was made in the seventh interspace of the left axilla. Novocaine anesthesia; 150 c.c. of air injected. Only slight negative pressure at the start, and last part of air injected under positive pressure. Complained of severe tearing pains in lower left chest during the injection.

December 1 (three days later). No hemorrhage since injection until the night of November 30, when there was a small hemorrhage during the night and a second at 11 A.M. today. Slight surgical emphysema about previous puncture site. 250 c.c. of air injected. No local anesthetic used. Most of the injection was made under positive pressure. Patient complained of severe pain in the left shoulder during and following the operation, lasting for several hours. Severe enough to cause attacks of syncope.

December 4. Patient's condition improved. No more hemorrhages, except slightly blood-streaked sputum. 300 c.c. of air injected, last 100 c.c. under positive pressure. Some pain in shoulder again caused.

December 7. No further hemorrhage. General condition seems slightly better; 150 c.c. of air injected, again causing severe pain. As there were no further hemorrhages, and the injections caused such severe pain, and as it seemed impossible on account of pleural adhesions to establish any extensive pneumothorax, further injections were not attempted.

Four months after the injection the patient died. Autopsy showed an extensive fibroid infiltration and a tuberculous bronchopneumonia of the left lung, and the pleura everywhere tightly adherent. No trace could be found of the pneumothorax, even in the area directly under the point where the puncture had been made. Evidently after the absorption of the air the pleural surfaces became adherent.

Summary. This case aside from the apparent control of the hemorrhages by the pneumothorax, is interesting in several particulars. There were evidently extensive pleural adhesions (a fact afterward established at autopsy), preventing any extensive collapse. The air, most of it forced in under positive pressure, must have broken up enough of these adhesions to form a pocket. This was probably the cause of the tearing pains felt in the lower chest on the first injection. In connection with the pains felt in the left shoulder during and subsequent to the injection most interesting is the work of J. A. Capps, of Chicago.[12] In several cases of pleural effusion, using a trocar through which a long blunt wire was passed, he investigated the pain sense by touching various parts of the pleura. When the arch of the diaphragm was touched pain was usually felt in the neck, at some spot, the position varying in different subjects, along the ridge of the trapezius muscle. In this case of pneumothorax under discussion the pain was referred to the upper part of the shoulder, a position nearly corresponding with that in some of Capp's subjects. It seems likely therefore that this is a correct explanation of his pain, that it was a referred pain due to a pulling on the arch of the diaphragm by pleuritic adhesions.

Case IX.—D. H., female, aged thirty years. Admitted January 27, 1912. Far advanced. Turban iii (R iii–L i). Duration of disease: since 1899 (thirteen years).

Symptoms. Fever (averaging 101° in P.M.), night sweats, gastric disturbance, expectoration (60 grams a day).

Complications. Toxic nephritis; laryngitis, with ulceration.

Physical Signs. Scattered infiltration throughout the right lung, most marked in the lower lobe. Slight changes in left upper lobe. Litten's sign present on both sides, more marked on left.

March 9. First injection of 300 c.c. of nitrogen into right side; pressure becoming neutral at this point. Evidently adhesions preventing further collapse. Temperature and expectoration both somewhat lower on succeeding days.

March 18 to April 23. Four injections of about 300 c.c. each.

Injections were discontinued after this, as there was no very noticeable result.

The physical signs when the injections were discontinued indicated a pneumothorax occupying lower right chest up to the first rib in front, and just above angle of scapula posteriorly. At present date (December, 1912) these signs have entirely disappeared. An *x*-ray plate also shows no remaining pneumothorax.

Summary. The patient did improve somewhat during the six weeks that injections were given, but as this improvement had

[12] An Experimental Study of the Pain Sense in the Pleural Membranes, Archiv. Int. Med., December, 1911.

apparently begun before the first injection, and has continued since they were stopped, it is doubtful whether the pneumothorax was an important element in the improvement, especially as no very complete collapse was obtained.

CASE X.—C. C. S., male, aged twenty-seven years. Admitted July 20, 1911. Condition: far advanced. Turban iii (R ii – L ii). Duration of disease: since August, 1910.

Symptoms. Constitutional symptoms not marked. Patient taking walking exercise up to two hours a day. Expectoration of about 100 grams a day. Improvement on ordinary hygienic dietetic treatment, had apparently reached a standstill.

Complication. Tuberculous laryngitis without ulceration.

Physical Signs. These indicated an extensive involvement of the left lung, with cavity signs in upper lobe, the base being comparatively clear. Litten's sign present. Signs of slight impairment of right lung anteriorly, with no definite signs of disease posteriorly. Apparently a favorable case for pneumothorax treatment.

January 25, 1912. First injection of 500 c.c. of air. Rather difficult to enter the pleural cavity with needle. Oscillations finally obtained on manometer, but with only slight negative pressure. The air was forced in under moderate positive pressure.

On the night following the injection the patient felt a severe pain in chest. Soon after this the neck began to swell and there was some difficulty in breathing. Examination showed surgical emphysema of the subcutaneous tissues of neck and face, and extending down on right chest wall. No emphysema about the puncture point. Emphysema cleared up in a few days.

The probable explanation of this condition is that there were pleural adhesions preventing a collapse of the lung, which also explains the failure to obtain a negative reading of the manometer. The 500 c.c. of air, forced in among the pleural adhesions under positive pressure, must have burrowed its way to the mediastinal region and there broken through the pleura into the mediastinum, whence it found its way, following the course of the trachea and large vessels, into the neck, spreading from there into the face and over the chest wall.

Summary. Unsatisfactory case on account of pleural adhesions. This case illustrates well one of the dangers of attempting to inject gas when there is not a negative pressure as revealed by the manometer. Oscillations on the manometer are not enough, in view of this experience, to justify injection. There must also be a definite negative pressure.

CASE XI.—A. S. H., male, aged thirty-eight years. Admitted April 9, 1910. Condition: far advanced. Turban iii (R iii – L ii). Duration of disease: since 1896 (fifteen years).

Symptoms. Severe cough and expectoration, averaging 220 grams a day the month previous to first injection. Slight afternoon temperature (100.4° to 100.8°). Patient at rest sitting up in a chair during the day and riding to meals.

Physical Signs. Extensive infiltration throughout the right lung, most marked in lower lobe. Possible small effusion at base (probably proved by result of injection, however, to be thickened pleura). Compensatory changes, in left lung. No present signs of activity in this lung, but probably scattered old lesions.

On account of extensive changes in the lower lobe the case did not seem an especially favorable one for pneumothorax.

July 30, 1911. First injection of 250 c.c. of nitrogen into the right pleura. Impracticable to inject more on account of positive pressure. Pleura found to be very thick. No change in condition noted.

August 8. Several attempts made to enter pleura in various localities, but impossible to obtain negative pressure on manometer.

On account of evident thickened adherent pleura, further attempts at pneumothorax were discontinued.

Summary. No improvement. Unsatisfactory case for treatment on account of pleural adhesions.

CASE XII.—A. M. P., male, aged thirty-one years. Admitted July 17, 1912. Condition: non-tuberculous case. Abscess of left lung. Duration: since February, 1912.

Symptoms. Periods of fever and night sweats, hemoptyses, expectoration varying in amount from 100 to 500 grams a day; loss of weight, 10 kg. (22 pounds).

Complications. Infection of sphenoidal sinus. Part of the expectoration is undoubtedly from this source.

Physical Signs. Slightly impaired resonance and modified breath sounds at the right apex, without rales. On the left, marked dulness, feeble breath sounds to the third interspace in front and middle of the scapula behind. Occasional rales over this area anteriorly.

Repeated search by concentration methods of examining sputum has failed to show bacilli. The von Pirquet is also negative. Case diagnosed as lung abscess and diagnosis confirmed by Doctor T. C. Janeway.

November 13. First injection of 500 c.c. of nitrogen into the left chest.

November 16. 600 c.c. injected.

November 23. 600 c.c. injected.

Expectoration has been slightly decreased following these injections. Running between 450 and 500 grams before, and now about 350 grams. Occasional hemoptyses and attacks of fever still continue (see Fig. 4).

December 12. Patient discharged. Condition: progressively less favorable. Expectoration as high as 500 grams.

December 29. Patient died at Presbyterian Hospital, New York. Autopsy showed lung abscess.

Summary. No improvement following collapse of lung in case of lung abscess.

FIG. 4.—Case XII. November 15, 1912. Pneumothorax occupying lower part of left chest. Lung partially compressed. Dense shadow of lung abscess extending out from hilus.

CASE XIII.—C. G., male, aged twenty-two years. Admitted February 26, 1911. Condition: far advanced. Turban iii (R i – L ii). Duration of disease: since November, 1909 (one year and nine months).

Symptoms. Excellent constitutional condition. Cough and expectoration (average 60 grams).

Physical Signs. Left lung: Extensive infiltration throughout, with probable small cavity anteriorly between third and fifth ribs. Right lung: Slight infiltration in upper lobe and at root.

Complications. Tuberculous laryngitis. Case appeared to be an excellent one for artificial pneumothorax.

July 30, 1911. First injection. Artificial pneumothorax attempted. Pleural cavity entered and negative pressure obtained. As soon as gas began to enter, patient complained of severe tearing pains in chest, becoming unbearable; therefore only 75 c.c. could be injected. As patient was not at all of neurotic temperament, these pains were thought to indicate pleural adhesions.

August 30. Second attempt at injection made, with same result. Further attempt therefore discontinued.

Summary. Inoperable case on account of pleural adhesions.

CASE XIV.—R. H. H., male, aged forty-five years. Admitted October 30, 1911. Condition: far advanced. Turban iii (R iii – L i). Duration of disease: since February, 1909.

Symptoms. Previous to admission to the Sanatorium had had attacks of pleurisy on right side, at one time with effusion. Expectoration about 50 grams a day. No marked constitutional symptoms except loss of weight.

Physical Signs. Extensive fibroid changes in right lung, with probable dry cavity in upper lobe, widespread adhesions at base, marked compensatory changes in left lung. Litten's sign absent on right side.

First injection, July 12, 1912.

The case did not seem very promising for pneumothorax treatment on account of the evidence of adhesions at the right base. On attempting to perform the operation this diagnosis was confirmed, it being found impossible to obtain manometer readings indicating an entrance of needle into pleural sac.

Summary. Inoperable case on account of pleural adhesions.

CASE XV.—C. N. N., female, aged thirty-one years. Admitted December 28, 1911. Condition: far advanced. Turban iii (R iii – L i). Duration: since 1905 (seven years).

Symptoms. Cough, expectoration (128 grams) fever (about 101° in P.M.), progressive loss of weight. Several attacks of pleurisy at onset of disease in 1905.

Complications. Laryngitis without ulceration. Probable tuberculosis of lower intestinal tract. Mild grade of nephritis.

Physical Signs. Physical signs indicate infiltration throughout right lung with probable cavity in upper lobe, few infiltration areas in left lung.

April 2, 1912. First injection. Attempt at pneumothorax. Satisfactory negative pressure not obtained. Slight respiratory oscillations; 100 c.c. of nitrogen cautiously injected.

April 6. Second attempt made, with no better result. Only 75 c.c. injected. Evidently extensive pleural adhesions.

Summary. Inoperable case on account of pleural adhesions.

CASE XVI.—J. C. W., female, aged forty-three years. Admitted August 2, 1907. Condition: far advanced. Turban iii (R iii – L i). Duration of disease: since 1899 (thirteen years).

Symptoms. Patient entered the Sanatorium in August, 1907, five years ago, in advanced condition, with high fever and expectoration. Had fever almost every day for two years. Since then the constitutional condition has improved remarkably, and for the past three years she has been, for most of the time, free of fever. Gain of weight of 17 kg. (37 pounds). Expectoration always high, about 120 grams during month previous to injection. Exercising about one-half hour, twice a day.

Physical Signs. Effusion on the right side at time of admission in 1907. Signs at time of injection indicated extensive fibroid infiltration throughout right lung, with destructive changes in upper lobe and thickened pleura and possibly some effusion below. Areas of infiltration and compensatory hypertrophy in left lung. Considered a rather unfavorable case before injection on account of probable pleural adhesions.

July 18, 1912. Attempt made at injection, but needle evidently entered thick pleural adhesions. No negative pressure or oscillations of manometer obtained. No gas injected.

Summary. Inoperable case on account of thickened adherent pleura.

General Summary. In 16 cases in which the treatment has been tried 2 have shown marked and apparently permanent improvement, 6 have shown temporary or slight improvement, in 1 case hemorrhages have apparently been controlled, in 1 case of lung abscess no improvement followed, while in 6 cases, on account of pleural adhesions, either no gas could be injected or not enough to produce any sufficient collapse.

THE DIAGNOSIS OF TUBERCULOSIS OF THE KIDNEY.[1]

By Floyd E. Keene, M.D.,

INSTRUCTOR IN GYNECOLOGY, UNIVERSITY OF PENNSYLVANIA; ASSISTANT GYNECOLOGIST TO THE UNIVERSITY HOSPITAL; GYNECOLOGIST TO THE CHESTNUT HILL HOSPITAL, PHILADELPHIA,

AND

John L. Laird, M.D.,

ASSISTANT INSTRUCTOR IN GENITO-URINARY SURGERY, UNIVERSITY OF PENNSYLVANIA; ASSISTANT SURGEON IN GENITO-URINARY DISEASES TO THE UNIVERSITY HOSPITAL; ASSOCIATE IN SEROLOGY, WILLIAM PEPPER CLINICAL LABORATORY, PHILADELPHIA.

It is only within comparatively recent years that tuberculosis of the kidney has become recognized as a distinct pathological entity amenable to treatment offering excellent chances for cure. While formerly looked upon as merely a terminal manifestation

[1] Presented before the Philadelphia Pathological Society, December 12, 1912.

of a general tuberculous infection or as a rare disease difficult to diagnosticate, modern methods of examination, together with an accurate knowledge of its mode of infection, pathology, and clinical course, have proved quite the reverse to be true.

Without going into a discussion of the possible avenues of invasion, we can say that it is now a generally accepted fact that the tubercle bacilli reach the kidney by way of the blood stream, and that this infection is primarily unilateral in the great majority of cases. Probably because of the intimate vascular connection a specific infection of the opposite kidney originates more frequently from its sister organ than from any other focus in the body. The course of the disease is progressive, passing from bad to worse, and, according to Israel, there is no authentic case on record which has been cured by other than surgical measures.

While primary tuberculous cystitis must be considered a pathological rarity, the bladder is commonly the seat of disease secondary to a renal infection. In the presence of a tuberculous cystitis, with its changes promoting incomplete evacuation as well as stenosis of the orifice of the sound ureter, an ascending infection of the second kidney, with the ureter as the avenue of entry, is likely to follow, as the experimental work of both Albarran and Baumgarten has demonstrated. Starting as a single or multiple focus of infection the further progress of the disease may produce changes altering not only the pathological but the clinical picture as well. Excluding miliary tuberculosis, which is merely the local manifestation of a general miliary tuberculosis, four types may be differentiated. Following an eruption of tubercles scattered more or less diffusely throughout the kidney, there may be little or no tendency to caseation, but rather to connective-tissue proliferation, transforming the kidney into a dense, irregular mass, at times impossible to differentiate from a neoplasm. Should areas of softening be present they frequently are surrounded by firm fibrous tissue impregnated with lime salts. The fibrous as well as the fatty capsule participates in this general tissue proliferation. A second type much rarer than the others is characterized by ulceration of the renal papillæ, so-called tuberculous papillitis which was first described by Israel, and due, in his opinion, to the passage of the bacilli through the tubules of the kidney, lodging at the papillæ, where they exert their destructive action. The type most commonly encountered is that presenting one or more cavities at the junction of the cortex and medulla, and not infrequently located at one or the other poles. These cavities vary in size, and may or may not communicate with the pelvis of the kidney. There is generally a chronic interstitial nephritis affecting the remainder of the renal parenchyma. In all these types, especially during the earlier stages of development, the kidney may present no gross enlargement; on the contrary, when extensive interstitial changes with fibrosis

are present the kidney may be smaller than normal. It is important to remember that the enlarged kidney may be the healthy one, the increase being due to compensatory hypertrophy incident to the added work which it must assume when the function of the opposite side is seriously impaired. The terminal stage of these various forms is seen in the tuberculous pyonephrosis, with almost or quite complete destruction of the renal parenchyma; a mixed infection may be engrafted on the tuberculous, transforming the kidney into an enormous pus sac. The ureter and bladder likewise participate in the tuberculous process, the infection being secondary to the primary renal focus, and of urogenic origin in most instances. Primary tuberculosis of the bladder is so rarely seen that its demonstration in the female sex means almost invariably that we have to deal with a primary focus in one or both kidneys. Changes in the ureter may be entirely absent, but, as a rule, some evidences of the tuberculous infection are to be found. These may consist merely of discrete tubercles scattered here and there along the mucous membrane, or, in cases of longer standing, there may be extensive thickening of the ureteral walls, with ulceration, connective-tissue proliferation, and contraction, forming one or more strictures which may completely occlude the ureter, resulting in the closed pyonephrosis. While this is but a cursory review of the pathology of tuberculosis of the kidney it represents the chief manifestations found clinically.

In spite of an enormous amount of literature and discussion on this subject, the diagnosis of renal tuberculosis is seldom made or even suspected by the general practitioner. The obsolete term irritable or nervous bladder remains a favorite expression of ignorance, dividing honors equally with false conceptions concerning the importance of uterine deviations in regard to the production of vesical irritability. An uncomplicated retroflexion seldom if ever produces urinary symptoms, and in the light of our present knowledge, acquired largely through the extensive use of the cystoscope, the term nervous bladder should be stricken from medical nomenclature. As a safe working rule, proven only by the rare exception, every bladder presenting symptoms should be considered the site of some organic lesion, and no effort should be spared to determine the exact nature of this lesion. We do not mean to imply that every irritable bladder is the seat of tuberculosis, but we do claim that only by following this rule can we hope to make the diagnosis sufficiently early to permit the application of proper surgical treatment.

We have reviewed the histories of twenty-five cases of tuberculosis of the kidney which have been admitted to Dr. Clark's service in the University Hospital, and the symptomatology which we shall give represents largely the summary of these cases.

In studying these histories, one is immediately impressed by

the rarity with which the symptoms are directly referable to the kidney itself; even in cases of enormous pyonephrosis or complete occlusion of the ureter the most the patient may experience is a dull, indefinite aching sensation in the lumbar region, and even this may be entirely absent. On the other hand, the pain may be so severe as to warrant the diagnosis of calculus; these acute attacks of colic may be due to sudden obstruction of the ureter by a thick plug of pus or may be associated with an extensive perinephritis, and especially periureteritis, upon which is engrafted an acute congestion following exposure to cold or at the time of the menstrual period. This pain is doubtless due to two factors, namely, increased tension upon the thickened, inelastic capsule of the kidney and partial or complete occlusion of the ureter incident to the swelling induced by increased vascularity.

The first and by far the most prominent symptoms of renal tuberculosis during the entire course of the disease are those referable to some abnormality in the function of the bladder. Starting, as a rule, with painless polyuria all degrees of dysuria are met, including the most intense strangury and even complete incontinence. Such vesical disturbances are not necessarily due to an organic lesion of the bladder itself; even in the earliest stages of renal involvement, with no extension of the process beyond the renal parenchyma, the vesical irritability may be intense. This is difficult to explain, but is supposed to be of reflex origin, due to the intimate nerve connections between the kidney, ureter, and bladder or to the irritating action of toxins eliminated in the urine. In our series of cases there were only two in whom some evidences of bladder involvement were not present, and in both there was increased frequency of urination but no dysuria. As a rule, by the time the patient presents herself for examination the bladder has become involved and the urinary disturbances are in more or less direct proportion to the degree of extension. These symptoms may be decidedly intermittent in their severity, with intervals of comparative comfort between the acute exacerbations. It is doubtless true that many cases reported as improved under tuberculin treatment are merely manifestations of the natural course of the disease.

In addition to these local symptoms are those commonly present in any chronic infection. While in the early stages the general health is but little if any affected, sooner or later indefinite gastrointestinal symptoms, especially nausea and vomiting, present themselves. There is a progressive loss in weight, and the patient tires easily on slight exertion. Contrary to the opinion so commonly expressed the temperature is normal, or at most shows only a slight evening elevation. Irregular fever, with chills and sweats, are evidences of a mixed infection or a more generally disseminated tuberculous process.

With the exception of the earliest cases, limited to a small abscess in the renal cortex, some degree of pyuria is the rule. The quantity of pus will naturally vary with the extent of involvement of the urinary tract; the greater the bladder involvement the greater the pyuria. In the presence of a mixed infection the urine is often loaded with pus, while in even advanced cases of pure tuberculous infection the pus is found in comparatively small amounts, may be entirely absent, or may be abundant at one examination, with only a moderate amount at the next. These variations are easily explained when we refer to the pathology. In the early cases there is no connection whatever between the tuberculous focus and the pelvis of the kidney. Or in the more advanced case, where are we dealing with a closed pyonephrosis, there is no communication with the bladder, and the pus cannot escape. The rapid change in the quantity of pus is more or less characteristic of renal tuberculosis, and is due either to the rupture of a cortical abscess into the pelvis of the kidney or to some factor promoting better drainage of an abscess which already communicates with the pelvis. While the discussion of the bacterial content of the urine is not in our province, we may be permitted to state the general working rule that pyuria without demonstrable bacteria, either by smear or culture, strongly suggests the possibility of a tubercular infection. Macroscopic hematuria is rarely seen even in the advanced stages of renal tuberculosis, and when present is usually of vesical rather than renal origin. In one form of the disease—namely, the tuberculous papillitis—profuse hematuria is characteristic. Albuminuria is usually present, but small in amount compared to the degree of renal involvement.

The objective findings must of necessity depend upon the type of disease as well as upon the degree to which the infection has extended to the bladder and ureter. In the early cases, in which the disease is limited to the renal cortex, physical examination will show no abnormalities whatever; usually, however, an enlargement of the kidney is manifest. Under normal conditions the right kidney can be palpated in 75 per cent. of women, consequently disease on this side is more easily demonstrated than when the left kidney is involved. Even a considerable enlargement on the left side may escape detection; this is especially true in those cases in which perinephritic thickening anchors the kidney in its high position. While the kidney may be diminished in size in the sclerotic type of the disease, this is rarely demonstrable clinically; the kidney either escapes detection entirely or a fixed mass can be palpated, consisting not only of kidney but its infiltrated fatty capsule. It must be remembered that a demonstrable enlargement does not necessarily indicate the diseased side, since this increase in size may be due to compensatory hypertrophy of the sound kidney. Tenderness, especially at the costovertebral angle, is

rarely absent, and is directly proportionate to the extent of perinephritis. When the disease has extended down the ureter there may be tenderness along its course, but even in those cases with marked thickening and complete stenosis we have never been able to say definitely that the ureter could be palpated by abdominal examination. Thickening of the vaginal portion of the ureter can be readily palpated, and its demonstration may be of importance in determining the side affected. While many authors lay great stress upon this point, and some even go so far as to state that it is pathognomonic of tuberculosis, too great dependence upon its significance will lead one astray, for we have been able to demonstrate ureteral thickening in several cases of pyelocystitis in which tuberculosis could be absolutely ruled out. Its presence is suggestive, but by no means characteristic.

The tuberculin reaction is of doubtful value; we have employed only the subcutaneous injection, and its results were considered significant only in the presence of increased kidney or bladder symptoms.

Lastly and by far the most important factor in the diagnosis is the cystoscope. It is often the only means at our command to determine the nature of the infection, and only by its use can we estimate the extent of involvement of the urinary tract, which is of the most vital importance in its bearing upon the advisability of surgical intervention. In women the diagnosis of vesical tuberculosis means almost invariably that the primary focus is in one or both kidneys; while in the majority of cases the changes in the bladder are characteristic, we occasionally meet instances of renal involvement, with a normal bladder picture, or, on the contrary, there may be such extensive disease of the bladder that the typical lesions of tuberculosis are masked. In the former the cystoscope is still a valuable aid in that it determines definitely the source of the pyuria; further, in the presence of vesical symptoms, with insufficient evidence in the bladder or its surrounding organs to account for these symptoms, tuberculosis of the kidney is a strong possiblity. While simple cystoscopy may not suffice in the far-advanced changes to warrant a diagnosis of tuberculosis, it at least shows that we are dealing with a severe infection which demands more detailed examinations to determine its exact nature. These include microscopic and bacteriological studies of the urine, ureteral catheterzation, and one or more of the functional kidney tests. In referring to the pathological changes in the bladder we follow the classification of Caspar, designating them as tuberculosis of the bladder and tuberculous cystitis; the former is a distinctly localized process, the latter general, involving not only the mucosa but often the muscularis as well. At the beginning of the disease the bladder as a whole shows little or no change from the normal; the characteristic picture is presented at the ureteral orifice and the mucosa surround-

ing it. Due to ureteral thickening the orifice is no longer linear but round, with edema, reddening, and superficial, irregular ulceration of its edges and adjacent mucosa. Further ulceration transforms the ureteral ostium into a large, crater-like opening, with rigid, unyielding walls covered with indolent granulation tissue. Contraction of the scar tissue of the ureter produces not only marked irregularity of the orifice, but actual retraction of the entire ureteral region, so that this portion of the bladder assumes a funnel-shape, with the larger opening directed downward. The orifice may also be surrounded by the so-called edema bullosum, or the picture may closely resemble a neoplasm when papillary alterations are present. Miliary tubercles are likewise found, usually situated in the trigone, but may be located in the fundus or sides of the bladder. In our series of cases tubercles were found only twice, which leads us to the conclusion that they are rather unusual manifestations. With further extension of the disease or in the presence of a mixed infection, which is so often present in the advanced cases, a more or less general cystitis ensues, with irregular ulcers and ecchymoses scattered here and there over the universally inflamed mucosa. Because of its long duration the infection involves not only the mucosa but extends into the musculature, thereby diminishing the size of the bladder until its capacity may be reduced to a few centimeters. Under these circumstances the ureteral orifices may be completely obscured and the typical pathology so masked that a diagnosis of tuberculosis is possible only by animal inoculation.

Having determined the nature of the infection, it is of equal importance to ascertain whether one or both kidneys are involved. In our opinion this can be accomplished only by catheterization of the supposedly sound side with a careful chemical, microscopic, and bacteriological study of the collected urine; a normal ureteral orifice does not prove that the corresponding kidney is not diseased, since the infection may not have extended beyond its original renal focus, nor is a normal functional test sufficient because the disease may not involve enough of the renal parenchyma to seriously interfere with its working capacity. Theoretically, catheterization of the sound ureter is objectionable because of the danger of promoting an ascending infection from an already diseased bladder; practically, however, this objection does not hold when care is exercised in passing the catheter directly into the ureter without touching the mucosa of the bladder and inserting the catheter only a few centimeters rather than into the pelvis of the kidney. The diagnosis is not complete until we have demonstrated not only anatomical but also functional integrity of the opposite kidney; the fact that the patient is free from the symptoms of renal insufficiency is certainly of the greatest value, but this must be further substantiated by the employment of one or more of the functional

tests. For this purpose we prefer indigocarmine, not only because of its simplicity and adaptability in even the most extensive forms of bladder infection, but also, and what is even more important, it affords a reliable index of the relative functional capacity of the sound kidney.

When these various examinations have failed to reveal the site of disease, the skiagraph may offer valuable information, as was our experience in one case which baffled the diagnosis by every other means. The cortical abscesses may cast a shadow when a deposit of lime salts is also present, but this is unusual, and therefore of but little practical importance. By means of ureteral catheterization and the injection of collargol the skiagraph may reveal not only strictures of the ureter, but also one or more cortical abscesses in communication with the pelvis of the kidney. In the one case referred to the small abscess was clearly shown and proved at operation.

This *resume* includes the more important clinical factors concerned in the diagnosis of tuberculosis of the kidney. While in many cases the diagnosis is plainly evident from the clinical findings, in others the nature of the infection is obscure and can be recognized only with the assistance of the laboratory. This phase of the subject will be covered by Dr. Laird.

The diagnosis of renal tuberculosis in the female is practically determined by positive tuberculous findings in guinea-pigs inoculated with the urinary sediment. In the male, however, the close relationship between the urinary and genital tracts renders the differentiation of the two, as the possible source of infection, necessary, and this lies principally in the clinical field. If by the clinical methods already described the kidneys have been proven normal, a thorough examination of the genital tract should be made to determine a possible involvement of the epididymides, vasa deferentia, seminal vesicles, prostate, or testes. As the kidneys are usually the primary foci of infection in the urinary tract, so the epididymides are the primary source of tuberculous infection in the genital tract. Primary tuberculous prostatitis, seminal vesiculitis, and orchitis have been reported, but these conditions were probably due to an indeterminate focus in the epididymis. As such foci may be clinically indeterminable, the secondary involvement of the other genital organs is naturally of importance in the diagnosis. The physical examination may reveal an enlarged, non-tender, non-painful, hard, nodular epididymis; thickening and induration of the vas deferens; a slightly nodular, non-tender, markedly indurated, and fixed prostate or seminal vesicle. The symptoms of tuberculosis of the genital tract are referable to disturbance of the genital function—namely, sexual erethism, discomfort or pain on ejaculation (which may, in acute cases, be slightly bloody), general weakness and nervousness after intercourse, leading finally to neuras-

thenia, usually sterility and later impotence. Pus may be absent from the urine in incipient cases of tuberculous epididymitis, but is usually present in cases with secondary involvement. The chronicity of the process is an important diagnostic point. The final diagnosis depends upon the finding of the tubercle bacilli in the seminal fluid or prostatic secretion.

LABORATORY METHOD.—Until the last few years the laboratory diagnosis of renal tuberculosis has depended upon the intraperitoneal or subcutaneous method of inoculation of rabbits or guinea-pigs. These methods consume about six weeks time or the time required for general tuberculosis to develop in the inoculated animals. To save this valuable time, Bloch, in 1907, advocated the inguinal method of inoculation, which requires only ten days for a positive diagnosis. Much has already been written upon this subject, but the advantage of the Bloch method as a time-saver over the old method, and the fact that the older, slower method is still quite generally used, especially in this country, were thought sufficient reasons for touching upon it once more in this comparative study.

The technique is as follows: A twenty-four hour specimen of urine is collected from the suspected case in a large sterile bottle, without the addition of a preservative. About 10 c.c. of urine from the lower portion of the specimen are placed into each of two centrifuge tubes and centrifugalized for from two to four hours, dependent upon the speed of the centrifuge, when the supernatant urine may be poured off, leaving the sediment in the bottom of the tubes.

From the sediment in one of the tubes, slide smears are made, which are then fixed, stained and examined microscopically for pus, blood, and bacteria, especially acid-fast bacilli. (Gabbett's method of staining the tubercle bacilli was employed in this work.) Pus is nearly always present in the urine in renal tuberculosis, varying greatly in amount, not only in the various stages of the disease, but also from time to time even in the late stages. This pus has, moreover, often a characteristic appearance both macroscopically and microscopically. The pus in tuberculous urine is grayish and granular, giving the urine when held to the light a ground-glass appearance in contrast to the soft yellowish appearance given by the pus in other conditions. The presence of blood, although occasional in renal tuberculosis, is more indicative of other pathological conditions of the genito-urinary tract. Acid-fast bacilli are nearly always present in the sediment in renal tuberculosis, but are frequently seen in the non-tuberculous conditions. The differentiation of the tubercle bacillus from the other acid-fast organisms, in spite of unceasing efforts at differential staining, is microscopically impossible. Although here as macroscopically the appearance of the pus and the bacilli is

sufficiently characteristic to arouse a suspicion which will afterward be proven a surety in a large percentage of cases. In contrast to the more or less discrete leukocytes comprising the pus seen in non-tuberculous genito-urinary affections, there are present large clumps of degenerated leukocytes, about the periphery of which will be found the typical slender, slightly curved, beaded rods, arranged in semiparallel groups, and giving one the impression that these organisms had a distinct part in bringing about the degeneration, whereas the other acid-fast organisms appear to have been accidentally dropped into a field of pus cells. The final diagnosis, therefore, must always depend upon animal inoculation.

For this purpose a suspension of the sediment in the second tube is prepared by shaking with 5 c.c. of sterile water. Two healthy, normal guinea-pigs are inoculated. The inguinal glands of the pigs are first slightly injured and thus rendered more susceptible to the attack of the tubercle bacillus, by pressing and rolling them between the forefinger and thumb for a few moments prior to the inoculation. 2½ c.c. of the prepared suspension, unheated, are then injected into each of the two pigs, subcutaneously, in the inguinal region directly below the glands. Pressure is again applied for a short time and repeated on the two days following the injection.

Ten days after the inoculation one of the two pigs is chloroformed and the inguinal glands on the injected side removed. These may be either sectioned, stained, and examined for tubercle bacilli, or, more simply and quite as reliably, finely macerated and pressed out between two microscopic slides, and fixed, stained and examined immediately.

In the majority of positive cases the microscopic examination of the inguinal glands results in the discovery of the tubercle bacilli in a few minutes. In some cases, however, in which the tubercle bacilli have been probably few in number or of low virulence the resultant inguinal involvement is so slight that the bacilli may escape detection by a cursory examination, and therefore a thorough search of every portion of the inguinal tissue should be made before a negative diagnosis is given.

In order to control the Bloch method of inoculation the second pig was allowed to live the required six weeks and then examined for general tuberculosis.

STATISTIC TABLE.

	Positive.	Negative.	Doubtful.
Clinical diagnosis	22	29	7
Bloch method	17	40	1
Subcutaneous method	17	40	1

Total, 58 cases. Positive by laboratory methods, 77.3 per cent.

There were 58 cases of suspected renal tuberculosis examined by the combined clinical, Bloch, and subcutaneous laboratory

methods. Twenty-two cases were proven, 7 by operation and 15 by subsequent clinical course, to have tuberculosis of the genito-urinary tract; 29 were proven, 3 by operation and 26 by subsequent clinical course, to be non-tuberculous; 7 cases were still clinically doubtful. By the Bloch method of inoculation, 17 cases were positive, 40 negative, and 1 doubtful, due to the premature death of the pig. By the subcutaneous method 17 were positive, 40 negative, and 1 doubtful, due to the same cause. In the clinically proven cases of tuberculosis, therefore, 77.3 per cent were positive by both laboratory methods. The 7 clinically doubful cases gave negative results by both methods. Of the clinically proven negative cases all but 1 gave negative results, and this was positive by both the Bloch and subcutaneous methods. This case was brought to operation on account of the positive laboratory findings; the apparently affected kidney was exposed and split, and showed, macroscopically, an interstitial nephritis and no evidence of tuberculous involvement. Two of the proven positive cases which gave negative laboratory results were closed cases, the ureter of the affected side being obstructed: 1 had advanced bilateral renal involvement, which shortly caused death; the other 2 were frank cases of unilateral renal tuberculosis. There were 2 clinically positive cases, each giving negative results by each of the two laboratory methods and positive by the other. Another positive case showed numerous tubercle bacilli in the inguinal glands of the pig at the expiration of ten days, and only one small focus of infection in the spleen of the other pig at the end of six weeks.

NOTE.—The Oppenheim method of hepatic inoculation was tried in a few instances resulting in every instance in the premature death of the pigs from septicemia.

CONCULSIONS.—1. The kidney is the primary site of disease in tuberculosis of the female urinary tract; as a rule the infection originates from a focus in some other organ and gains entrance to the kidney by way of the blood stream.

2. The pathology varies greatly in kind as well as in degree, but a definite type usually predominates, altering both the pathological and clinical pictures.

3. Subjective symptoms referable to the kidney disease are by no means characteristic; they are often entirely lacking, may be expressed by a dull, aching sensation in the lumbar region or by attacks of colic resembling calculus.

4. The most prominent symptoms are those referable to deranged bladder function; starting with painless polyuria, all degrees of dysuria are met, including the most intense strangury and even incontinence. These symptoms may be decidedly intermittent in their severity, with intervals of comparative comfort. A cystitis which does not readily yield to the usual appropriate measures should arouse the suspicion of renal tuberculosis.

5. Some degree of pyuria is the rule; hematuria the exception. Intermittent pyuria suggests tuberculosis of the kidney. Pyuria without demonstrable bacteria by smear or culture in a catheterized specimen is likewise suggestive. Albuminuria is usually present, but small in amount compared to the degree of renal involvement

6. In the absence of mixed infection the temperature is normal or shows only a slight evening elevation; irregular fever with chills and sweats is evidence of a mixed infection or a more generally disseminated tuberculous process.

7. The palpatory findings are dependent upon the type and extent of the pathological changes. While enlargement of the diseased kidney is usually manifest, it is important to remember that compensatory hypertrophy of the kidney may be given erroneous conclusions in determining the diseased organ. Thickening of the vaginal portion of the ureter is of value in diagnosis, but by no means characteristic of tuberculous infection.

8. The tuberculin reaction is of doubtful value; the subcutaneous injection should be employed and its results are significant only in the presence of increased kidney or bladder symptoms.

9. By far the most important agent in determining the diagnosis is the cystoscope, which in the majority of cases shows a picture so characteristic that the nature of the infection is at once recognized. Only by its use can we decide the extent of disease as well as the condition of the opposite kidney as regards both its anatomical and functional integrity.

10. The diagnosis of renal tuberculosis should be made in every suspected case by the combined clinical and laboratory examination.

11. The Bloch method of inoculation of guinea-pigs should be used, because it is equal in reliability to the older method, and the diagnosis may be made in at least 77.3 per cent. of cases in ten days compared to six weeks by the subcutaneous or intraperitoneal methods, which should also be used as controls.

12. A positive laboratory result by either method determines the diagnosis of tuberculosis of the genito-urinary tract; of renal tuberculosis in the female, the exact focus in the male to be determined by additional clinical and laboratory means.

13. A single negative laboratory result, regardless of thoroughness of examination, does not determine an absolute negative diagnosis of renal tuberculosis, as the manifestation of this disease is essentially intermittent. Negative results obtained in three successive weekly examinations should, however, bear considerable weight in the diagnosis.

INVAGINATION OF MECKEL'S DIVERTICULUM ASSOCIATED WITH INTUSSUSCEPTION: REPORT OF A CASE, WITH A STUDY OF RECORDED CASES.

By Arthur E. Hertzler, M.D.,
and
Edward T. Gibson, M.D.,
Kansas City, Missouri.

Meckel's diverticulum has long been known as a cause of abdominal disorders. A common source of disturbance is obstruction caused by the constriction of coils of intestine about the diverticulum when both its ends are attached. When the distal end is free the diverticulum itself not uncommonly becomes in some manner twisted upon itself or strangulated.

A less common source of trouble is inversion of the diverticulum into the lumen of the bowel, thereby causing obstruction to the intestine. In a number of instances inverted diverticula are associated with intussusception of the intestine. The diverticulum may pass into an intussusception without itself becoming inverted. Which of these events is cause and which effect is a matter of controversy that will later receive attention. It is the purpose of this paper to collect all the cases of inversion combined with intussusception recorded in the literature. We are able to add one of our own. On the basis of the data thus collected the question of pathogenesis will be discussed, the problem of the pathology stated, the results of treatment as heretofore carried out summarized, and the problem of the best method of treatment presented for the critical consideration of the reader. Our case is as follows:

F. M. W., aged nineteen years. Two years ago the patient had a severe attack of abdominal cramps. He attributed it to eating raisins. The attending physician at his first visit found nothing, but an examination made a day later revealed a tumor immediately below the umbilicus. This was supposed by his physician to be a mass of raisins and he manipulated it with his fingers in order to break up the lump. The cramps subsided and flatus and stool passed on the next day. The patient was free from any complaint from that time until December 18, 1912, when he became chilly and nauseated while loading a wagon. The two days following he felt much improved. On the third day he ate a hearty breakfast and later a ham sandwich, and took a small drink of whisky, to which he was not accustomed. He immediately began to have cramp and walked about to lessen the pain. After a few hours he vomited freely. The pains increased during the afternoon, and he rolled about from pain, and a doctor was summoned. Morphin was administered hypodermically and was repeated the following day.

Many enemas were employed during the following days, but pain and vomiting continued. During this period the physician was able to palpate a tumor to the right of the median line. On Friday the enema brought away a piece of the meat eaten on the Sunday previous; this gave some relief, and a little supper was eaten. On the following day he became worse again and was brought to the Halstead Hospital Saturday afternoon, with the diagnosis of intestinal obstruction. On examination the abdomen was but little sensitive, and there was no rigidity. Two hypodermics of morphin had been given during the day, which made this negative evidence of little value. There was moderate distention; no dulness in either flank; the tongue was dry and coated; there was no evidence of impending collapse. Pulse, 144; temperature, 97°; respiration, 24.

The abdomen was opened in the median line below the umbilicus. When the peritoneum was opened about a quart of straw-colored fluid escaped. The intestinal coils appearing in the incision were injected and much distended. There was no paralysis. The ileocecal portion of the intestine was at once sought and was found lying over the kidney. It presented a tumor. When the tumor was drawn into the wound it was seen to be an intussusception through the ileocecal valve, about twelve inches long, with a distinct tumor at its upper extremity. The tumor was thought to be a polyp which had produced the inversion of the gut. When the intussusception was reduced by traction and pressure on the tumor a dimple remained over the base of the supposed polyp. This made it obvious that the tumor mass was an inverted Meckel's diverticulum, with a thickened apex. By careful pressure the diverticulum was restored to its former position. The diverticulum was nearly the diamater of the gut from which it sprang, and was about two and a half inches long. The mass in its apex was about the size of a hulled walnut. The diverticulum was clamped just below the solid mass and a mattress suture passed on the ileal side of the clamp. The clamp was removed and the gut severed, the edge being cauterized with carbolic acid and iodin. This raw end was then inverted into the lumen of the gut. The contracture of the walls of the intestine after the suture line had been inverted resulted in narrowing the lumen of the gut more than had been intended. No evil resulted, however, as the lumen remaining was the size of a finger, but looked small in contrast to the adjoining dilated gut. The cecum was replaced and the loop of ileum containing the stump of the diverticulum was pulled over above and distal to the cecum. An inch stab opening was made in the side just above the crest of the ilium. A small, flat gauze pack was placed over the ileum and a drainage-tube below it. The incision in the median line was closed completely.

Following the operation the patient awoke quickly, and at 6 P.M.

his chart showed pulse, 132; temperature, 100.8°; respiration, 28. At 9 P.M.: pulse, 124; temperature, 101°; respiration, 28. He attempted to vomit and his stomach was emptied by lavage of a large amount of greenish fluid. Flatus was expelled late in the evening following an enema. There were emesis and repeated gastric lavages in the days following. On Tuesday, the third day, there was free bowel movement, with much flatus, and the patient complained of hunger. On the fifth day, Friday, the chart showed pulse, 92; temperature, 99.2°; respiration, 24. Saturday: pulse, 78; temperature, 99.4°; respiration, 24; on the seventh day: pulse, 68; temperature, 98.4°; respiration, 20. During the first two days there was a profuse drainage of cloudy serum from the drainage opening; this became reduced at the end of the second day, and the drains were removed. The skin of the entire central incision opened on the sixth day, and a considerable amount of pus was expelled.

Pathologic examination of the specimen: The part removed consisted of a mass about the size of a hulled walnut, with a flange of diverticular wall below it in which the muscular and mucous coats could be readily made out. On section the mass was seen to be composed in part of blood clot, giving the appearance of a submucous accumulation of blood of some days' duration. At the apex of the tumor immediately beneath the peritoneum was a cap 3 or 4 mm. thick, which was pearly white and resembled when cut the section of a skin papilloma. Microscopic examination showed the submucous thickening was due to an old blood clot. Toward the opening of the diverticulum the mucosa was normal, but at the apex it was continuous with the white thickened cap. The latter proved to be composed of glandular tissue arranged in two distinct layers; an inner, made up of Brunner's glands somewhat irregularly disposed; and an outer, which resembled the benign adenomas so often found in the intestines. This arrangement suggested strongly the aberrant masses of pancreatic tissue, which have often been reported present in Meckel's diverticula, and particularly the case in which Küttner observed both Brunner's glands and aberrant pancreatic tissue. The fact that in our case some of the misshapen Brunner's glands terminated in the adenomatous portion, raises the question whether the so-called pancreatic tissue may not in reality have been aberrant intestinal glands. The cases in the literature are, however, given with too little detail to permit one to do more than speculate in this direction.

The cases which we have been able to find reported in the literature as invagination of a Meckel's diverticulum with intussusception are some of them so incomplete as to be mere statements that such cases were observed. The reports of others show that they do not belong to the group of cases under consideration. A third group is reported fully enough to permit a judgment of the anatomic char-

acters of the lesion and to give a picture of the clinical course. The last group only will receive detailed consideration, though a list of the incompletely reported cases will be appended.

Case 1.—1894. Studsgaard, *Centralbl. f. Chirurgie*, 1894, xxi, 934.

Male, aged thirty-seven years. At operation there was found peritonitis and invagination of the bowel, the latter containing an introverted Meckel's diverticulum. A section of intestine was removed and death followed the same day.

Case 2.—1898. De Quervain, *Centralbl. f. Chirurgie*, 1898, xxv, 839.

Male, aged sixteen years. Patient was seized with severe abdominal pain and vomiting, without known cause. There were numerous borborygmi, but no passage of gas. No blood in stool. There was palpable resistance in the ileocecal region, but no tumor. Moderate distention and diffuse tenderness. Laparotomy revealed a gangrenous intussusception, which was removed entirely and an artificial anus produced. Death followed in a few hours. The part removed contained an invaginated Meckel's diverticulum 5 cm. long.

Case 3.—1898. v. Stubenrauch, *Centralbl. f. Chirurgie*, 1898, xxv, 137.

Female, aged five and a half years. Patient became acutely ill with severe colic and tenesmus, with bloody stools. On second day she had vomiting. On the fifth day she was admitted in a collapsed condition. The abdomen was moderately distended, sensitive to pressure, and especially prominent below the navel. At operation an intussusception of the ileum was found, 10 cm. from the ileocecal valve. Resection; death in two hours. The intussusception was gangrenous and contained an invaginated Meckel's diverticulum 5½ cm. long.

Case 4.—1898. Erdmann, *Ann. Surg.*, 1900, xxxi, 186; *New York Med. Jour.*, April 16, 1898.

Male, aged nine years. Illness began with colicky pains in right side of abdomen, then vomiting and bloody stool. The next day tenesmus, and on the second day severe shock and a palpable tumor extending from the right iliac fossa to the tenth costal cartilage. The abdomen was distended, tympanitic, and tender. At operation an intussusception was found with its apex within six inches of the ileocecal valve. It was irreducible, gangrenous, the intestines were deeply engorged, and there was a quantity of pus in the abdominal cavity. Resection, end-to-end anastomosis; death in four days. At the end of the invagination there was an introverted Meckel's diverticulum.

Case 5.—1898. Moroni, *Virchow's Hirsch Jahresbericht*, 1898, xxi, 289. Male, aged twenty-six years. Onset acute; pain and vomiting. Had previous operation for ileus due to axial torsion.

Renewed obstruction, death. Pathology, a complete ileal intussusception caused by inversion of Meckel's diverticulum, which contained a fibrous polyp the size of a cherry.

Case 6.—1899. Strauch, *Zeitschr. f. klin. Med.*, 1899, xxxviii, 465; *Hildebrandt's Jahresbericht*, 1899, v, 627.

Female, aged six years. Had been subject to severe attacks of colic for years. Suddenly had complete obstruction and was operated after thirty-six hours. There was an invagination of the intestine 15 cm. long, the apex of which consisted of a Meckel's diverticulum completely invaginated; resection; death.

Case 7.—1899. Robinson, *British Med. Jour.*, 1899, ii, 1416.

Male, aged five years. Patient had pains in belly, which became localized about the umbilicus during the night, and were accompanied by bilious vomiting. There were hiccough and thirst, but no distention. The next afternoon the pain became continuous, and distention appeared and became worse in the evening. There was a little blood in the enema fluid. There was no rigidity nor special tenderness. There was a lump over Poupart's ligament, which was comparatively dull on percussion, and on palpation by rectum there was a cylindrical mass three inches long in Douglas' pouch. Upon incision clear fluid escaped. The main invagination was easily reduced, but the introverted Meckel's diverticulum had to be excised. The patient collapsed and died in two hours after the operation.

Case 8.—1899. Brunner, *Beitr. z. klin. Chir.*, 1899, xxv, 344.

Male, aged four years. There had been no previous illness. The onset was sudden, with abdominal pain. In a few hours there was a bowel movement, followed by considerable hemorrhage, after which the pain became continuous, and the constipation absolute, notwithstanding frequent enemas. The abdomen was distended, but not rigid. There was dulness on percussion, from the right iliac fossa to the region above the pubes, and in the latter situation a hard nodular mass could be felt. Operation was performed three days after the beginning of the illness. An invagination of the ileum extending into the cecum was found, which, being irreducible, was resected. The operation lasted two and a half hours. The patient recovered. Within the invagination was an inverted Meckel's diverticulum, with a tumor at its apex. The tumor lay immediately beneath the serosa, unattached to the intestinal wall, and was formed of two parts, a superficial layer of fat and a deeper portion, which was glandular, resembling the pancreas.

Case 9.—1900. Bayer, *Centralbl. f. Chirurgie*, 1900, xxvii, 1138.

Male, aged two and a half years. Illness began with a bowel movement attended by severe pain, which was followed by obstruction. A tumor was palpable in the ileocecal region, and later in the region of the hepatic flexure. At operation the bowel was disinvaginated without difficulty. There became apparent a

dimple, 15 cm. from the valve, which marked the base of a Meckel's diverticulum 3 cm. long, which was invaginated into the lumen of the gut. This was everted and its lumen obliterated by a series of puckering stitches; recovery.

Case 10.—1900. Hohlbeck, *Arch. f. klin. Chir.*, 1900, lxi, 1.

Male, aged eighteen years. Abdomen somewhat distended, but not tender. Vomiting of yellow fluid. The flanks were dull on percussion. No tumor was palpable until the patient was in narcosis, when a lump was found in the ileocecal region. At operation an ileocecal invagination was found and easily reduced. A Meckel's diverticulum was present, and had been drawn into the intussusception. The mucosa was separated from the muscle of the diverticulum and was invaginated, forming a floating tumor as large as a walnut in the lumen of the bowel. The diverticulum was excised. Death on the second day.

Case 11.—1901. Eve, *British Med. Jour.*, 1901, ii, 582.

Male, aged thirteen years. Illness began twenty-eight days before operation. Upon incision an intestinal invagination appeared and was resected. The patient died. At the apex of the intussusception was an invaginated Meckel's diverticulum.

Case 12.—1901. Pitts, *British Med. Jour.*, 1901, ii, 578.

Male, aged eighteen years. The patient, after eating a pint of cherries, had severe abdominal pain, which at first improved, but after five days became worse. The abdomen became distended, and there was some dulness and resistance in the cecal region. At operation an intussusception was found in the hepatic region. The gut was opened and emptied of a pint of fluid. A Meckel's diverticulum had invaginated into the intestine, and was reduced by finger through an incision. The diverticulum was two feet from the valve. Recovery.

Case 13.—1901. Morison, *Lancet*, 1901, ii, 1047.

Male, aged five years. The patient was seized with acute abdominal pains, coming on in paroxysms and with vomiting. Blood was passed by rectum. There was a sausage-shaped tumor in the left iliac region. At operation an intussusception of the lower ileum was found and reduced. It contained an inverted Meckel's diverticulum, which was removed. The child recovered.

Case 14.—1902. Travers, *Lancet*, 1902, ii, 146.

Male, aged ten years. The patient suffered repeated attacks of abdominal pain in the right side and vomiting. The abdomen was flat, except for a prominence about McBurney's point, where a tumor about 2 x 1 inch in size was palpated. It later disappeared, giving place to an indefinite mass. At operation the ileum was found invaginated three inches into the colon, and was reduced with some difficulty. At its upper end was a lump as large as a filbert, which proved to be an inverted diverticulum, three-quarters of an inch long. Recovery.

Case 15.—1902. Wainwright, *Ann. Surg.*, 1902, xxxv, 32.

Male, aged seventeen years. Illness began six days before admission, with loss of appetite, sense of fulness after eating, and constipation. Worked for five days. On the fifth day he was seized with severe epigastric pain and began to vomit. Enemas returned bloody. On admission to the hospital the abdomen was retracted and board-like, tender over lower part, but no tumor was palpable. Upon incision clear fluid gushed out and an intussusception three inches long was found three feet from the valve, which had at its apex an invaginated Meckel's diverticulum about an inch long. It was removed. Recovery.

Case 16.—1903. Terry, *Lancet*, 1903, i, 961.

Male, aged twelve years. The patient had first abdominal discomfort, soon followed by severe attacks of pain, which was most acute below and to the right of the umbilicus. Stools were loose, watery, and blood-stained. Distention was slight. A sausage-shaped tumor was palpable, running upward toward the liver. It became harder during the attacks of pain, and varied in size from time to time. At operation an invagination, twelve inches long was found, at the apex of which was an inverted Meckel's diverticulum six inches long. Recovery.

Case 17.—1903. Zum Busch, *Centralbl. f. Chirurgie*, 1903, xxx, 733.

Male, aged twenty-one years. Patient had dull pain in umbilical region for fourteen months. The present attack began suddenly, with severe pain, fluid stools, and tenesmus. Later there was almost constant vomiting and blood per anum. The right rectus muscle was tense, and a tumor the size of a child's head was palpable in the ileocecal region. At operation an ileocecal invagination was reduced with much difficulty. There remained a tumor in the ileum, wherefore a meter of intestine was resected, with lateral anastomosis. The tumor proved to be an invaginated Meckel's diverticulum, with a lipoma the size of a hazelnut at its apex. The patient recovered.

Case 18.—1903. Dobson, *Lancet*, 1903, i, 1161.

Male, aged four and a half years. Illness began with acute abdominal pain, vomiting, and discharge of blood and mucus from bowel. In thirty-six hours the vomiting had ceased, the pain became constant, with pulse 120 and temperature normal. There was a soft, tender, movable swelling in the right iliac region, extending upward to the right costal margin. At operation the same evening an ileocecal intususception was found, with a pedunculated swelling at the apex. Corresponding to this on the surface of the gut was a dimple into which a small mesentery passed. The swelling was an invaginated Meckel's diverticulum. Resection, Mayo Robson bobbin; recovery.

Case 19.—1904. Cawardine, *Lancet*, 1904, i, 505.

Child, aged fourteen months. At operation two days after beginning of symptoms an intussusception was found which had just entered the colon. One invagination was reduced and was found to contain a second invagination, within which was an introverted Meckel's diverticulum. The diverticulum was fifteen inches from the valve. The patient died in collapse.

Case 20.—1904. W. Watson Cheyne, *Ann. Surg.*, 1904, xl, 796.

Male, aged nineteen years. The patient had indefinite abdominal pain for two years. Several of the later attacks were attended with vomiting and diarrhea. The vomitus was greenish or yellow. On admission the abdomen was slightly distended. A week later a distended loop of bowel appeared in the left iliac region, which later appeared as a definite tumor. In the evening the bowels moved and contained no blood. At operation, three days later, an intussusception was found in the pelvis. It was eighteen inches long and was easily reduced. A second invagination presented itself and was easily squeezed out. It proved to be an inverted Meckel's diverticulum. This was resected and a lateral anastomosis done. The gut at the site of the diverticulum contained a longitudinal constriction. The patient recovered.

Case 21.—1907. Coffey, *Ann. Surg.*, 1907, xlv, 42.

Male, aged seven years. There was a history of repeated attacks of cramps beginning at two years, recurring every month, and sometimes more often. The cramps were always accompanied by bloody stools. The present attack began with severe pain and frequent vomiting during the first day. The condition improved, but abdominal tenderness continued. The patient was up a portion of the second day and remained well until the fifth day, when severe symptoms returned. On the sixth day the child entered the hospital. There was no distention. On the right side a mass was palpable, extending under the ribs. At operation reduction proved impossible, and the invagination was resected. There was an inverted Meckel's diverticulum at the apex of the intussusception. The patient recovered.

Case 22.—1907. Jäckh, *Deutsch. Zeitschr. f. Chir.*, 1907, lxxxvii, 192.

Female, aged thirty years. The patient had been ill for six months, with cramping pains almost daily. They had become worse in the last three weeks, and were occasionally accompanied by vomiting. There was moderate distention and visible peristalsis in the middle of the abdomen. There was no dulness nor tenderness. The day following the examination there was a bowel movement. Seven days later tumor was felt at the left of the uterus. At operation an invagination was recognized and was easily reduced, but a nodule as large as an egg remained about one meter above the valve. This portion of the gut was resected. The nodule

proved to be an invaginated diverticulum, which was necrotic at the extremity. The lumen of the diverticulum had become closed, and the gut proximal to the diverticulum was double the thickness of the distal part. The patient recovered.

Case 23.—1907. Bidwell, *Lancet*, 1907, ii, 682.

Male, aged three and a half years. The patient was born with an umbilical hernia, which was repaired at the age of one year. Severe hemorrhage from the bowel four months before present attack. There had been repeated attacks of pain, which came on at intervals of one week. They began in the morning and passed off after two hours. Final attack began as the others, but failed to pass off. Vomiting appeared and a tumor was palpable in the right lumbar and hypochondriac region. At operation an intussusception was found involving the large intestine to the middle of the transeverse colon; it was black and edematous, but was viable and was reduced. Four weeks later it was necessary to repeat the laparotomy. An irreducible invagination of the small intestine was found and resected. The specimen contained an inverted Meckel's diverticulum. Recovery.

Case 24.—1907. von Mandach, *Lancet*, 1907, ii, 1733.

Male, aged two and a half years. No history of previous trouble. The child fell ill with slight dyspeptic symptoms. On the seventh day the bowels became completely obstructed, meteorism developed, and operation was performed. There was a double ileocecal invagination, with an introverted Meckel's diverticulum at the apex. The invagination was reduced, the diverticulum everted, and its lumen closed by purse-string ligatures. Recovery.

Case 25.—1907. Kopyloff, *Mediz. Obosrenje*, Band lxviii, abstracted in *Hildebrandt's Jahresbericht*, 1907, xiii, 765.

An obstruction of the bowel originating from an inverted Meckel's diverticulum. A portion of intestine 60 cm. long was resected. Patient recovered.

Case 26.—1908. Brin, *Bull. et mém. Soc. de chir.*, 1908, xxxiv, 1267.

Female, aged thirty-nine years. The patient had been having attacks two or three times yearly for twelve years. During the past year there had been tenderness between attacks. A pelvic tumor was palpable and was thought to be an inflamed salpinx. Supravaginal hysterectomy was performed. Eight days later she had an attack of acute obstruction. The intussusception was reduced, and an inverted Meckel's diverticulum was evaginated and resected. The patient recovered.

Case 27.—1908. Gray, *Ann. Surg.*, 1908, xlviii, 801.

Male, aged eight years. At five years there was an attack of abdominal pain, with passage of blood by rectum. The present illness began with pain in the region of the umbilicus. There was temporary improvement, but after two days, following a bowel

movement produced by licorice powder, violent pain returned. On the fifth day there was increased pain and absolute constipation, followed the next day by vomiting. No blood was passed by rectum. The abdomen was distended, especially above the navel, which was raised, and at the apex of a dome. There was no rigidity nor tenderness. Under anesthesia a tumor was palpable under the liver. At operation a good deal of straw-colored fluid was found in the abdomen. There was an ileocecal invagination, which was removed from the cecum. The enteric part was irreducible and was resected. The patient died fifteen hours afterward. The resected portion contained an inverted Meckel's diverticulum, at the base of which the intestine was considerably narrowed.

Case 28.—1908. Kothe, *Deutsch. Zeitschr. f. Chir.*, 1908, xcv, 286.

Male, aged twenty-three years. The patient had an attack six months previously. The final attack began suddenly, with pain, vomiting, and chill. Vomiting did not recur. The pain was most severe between the umbilicus and symphysis. There was passage of neither feces nor flatus. When admitted to the hospital on the fourth day the abdomen was not distended, but was slightly tender. The next day tympany became marked, vomiting was violent, and the general condition was much worse. At operation a moderate amount of serosanguinolent fluid escaped from the abdomen. An intussusception was found in the ileocecal region, and as it was irreducible it was resected. The intestinal contents were allowed to flow out of the free end of the gut, and then an end-to-end anastomosis was done. The patient recovered. At the tip of the invaginated diverticulum was an infarcted polyp 6 cm. long.

Case 29.—1908. Kothe, *loc. cit.*

Male, aged seven months. Illness began three days before operation. Vomiting occurred once on the second day. Enemas were used without result; in one the water was returned bloody. There was no tympany, but the abdomen was generally tender, particularly so in the ileocecal region. There was no dulness nor tumor. Under anesthesia a tumor was palpable in the right lower quadrant. At operation a moderate amount of serous exudate escaped. The ileocecal tumor was recognized as an intussusception, which was pushed into the ileum, but the gut ruptured from the manipulation, and was therefore resected. The cut ends were sewed into the abdominal incision. The patient died from exhaustion. There was no peritonitis. Examination of the specimen showed a diverticulum 2 cm. long, which was inverted into the ileum.

Case 30.—1908. Delore et Leriche, *Revue de Chir.*, 1908, xxxviii, 39.

Male, aged six years. Patient had had several attacks of ob-

struction in last year. July 22, 1907, had vomiting of bile, colicky pains, no passage of gas, or feces. Next day pulse was 80, temperature was 38.5° C. and there was a tumor in the right iliac region. July 25, pulse, 115; temperature, 37.8°; violent colicky pains, bilious vomiting, complete obstruction; no melena. The abdomen was distended and there was a mobile tumor in the left iliac region. At operation (third day after beginning) there was a large quantity of liquid in abdomen. The invagination could not be reduced, was resected, and the intestine joined end-to-end with a Murphy-Villard button. Patient died forty-eight hours later. The piece resected was 40 cm. long, and the intussusceptum was 15 cm. long. The mucosa was gangrenous. There was a depression in the serous surface into which a probe could be thrust 5 or 6 cm.—an inverted Meckel's diverticulum.

Case 31.—1909.—Busch, *Deutsch. med. Woch.*, 1909, xxxv, 1369 and 1370.

Child, aged seven years. The patient came to clinic on the third day of the illness. At operation an invagination was found which reached from 50 to 60 cm. above the ileocecal valve to the hepatic flexure. At the end of the intussusception was an inverted Meckel's diverticulum with a hard nodule as large as a hazel-nut at the apex which proved to be an accessory pancreas. The diverticulum was resected and the patient recovered.

Case 32.—1909.—Riedel, *Deutsch. med. Woch.*, 1909, xxxv, 1655.

Female, aged twenty-five years. The attack began suddenly with severe pain in abdomen and vomiting. There was tenderness at first below the flanks. The diagnosis was perforative peritonitis, with intestinal paralysis. At operation an invagination 20 cm. long was found in the pelvis and was resected. The patient died at the end of the operation from heart failure. The diverticulum was found inverted and partly gangrenous.

Case 33.—1911. Mühsam, *Berl. klin. Woch.*, 1911, xlviii, 1089.

Female, aged five years. The patient had had two attacks of obstruction, which were cured by enemas. The present attack began with vomiting and obstruction. There was a hard, sausage-shaped movable tumor to the right of the navel. There were 30,000 leukocytes. At operation there was an invagination reaching to the hepatic flexure, which was reduced with some difficulty. 20 cm. from the valve was a diverticulum the size of a little finger, invaginated into the bowel. It was everted and resected. The patient recovered.

Case 34.—1912. Drummond, *Ann. Surg.*, 1912, lv, 404.

Male, aged twenty-nine years. Admitted July, 1909 for hemoptysis. He was discharged but soon returned complaining of colicky pains in abdomen, epigastrium, and left hypochondrium. He had occasional griping pains until November, 1910. In December of

same year had renewed abdominal pain with tenderness and distention in the epigastrium. In the following February, after sudden pain in the abdomen with vomiting, a mass appeared in the lower abdomen which increased in size and became harder during the paroxysms of pain. He passed a pint of blood per rectum. Operation February 6, 1910. There was some free fluid in the abdomen and an intussusception four inches from the ileocecal valve. It was easily reduced but a lump remained within, and a portion of intestine was therefore resected, with end-to-end anastomosis. Death February 14, from peritonitis from leak in suture line. Specimen showed a diverticulum three and one-half inches long with a constriction of the gut at the point of its attachment.

Case 35.—*Loc. cit.*

Female, aged three years. The child had an attack every six weeks, for the last nine months, which were relieved by enemas and castor oil. Duration of the present attack, one week. Two hours after breakfast the patient was seized with sudden severe pain about the umbilicus followed by vomiting. No flatus nor feces was passed for two days. On admission pulse was 126; temperature, 99.8°; upper abdomen was distended and peristaltic waves were visible in the region of the umbilicus on right side. There was no rigidity nor tumor. At operation, an intussusception was found and easily reduced except where the diverticulum was inverted into the gut. Diverticulum was reduced and excised. Child died twelve hours later. Diverticulum was one and one-fourth inches long and contained an accessory pancreas.

Case 36.—*Loc. cit.*

Male, aged fifteen years. Four days before admission the patient had an attack of pain in lower abdomen, with nausea and vomiting. Next day bowels moved and he was better. In the evening severe pain and vomiting returned with relief next morning. On the second day following when admitted, he had slight pain and distention, no tumor nor dullness. There was tenderness in left side. At operation an irreducible intussusception of the small bowel was found and resected, with end-to-end anastomosis. Death shortly afterward. At apex of intussusception was a Meckel's diverticulum four and one-half inches long, completely gangrenous.

Case 37.—*Loc. cit.*

Male, aged eleven years. Three days before admission he complained of sudden pain in epigastrium followed by vomiting. No movement of the bowels occurred for two days. Abdomen was distended, tympanitic, and tender. A tumor was palpable by rectal examination. At operation, free fluid was found in abdomen, and an intussusception of small intestine in pelvis. Resection was followed by death. A Meckel's diverticulum one and one-half inches long was found completely inverted and gangrenous.

Case 38.—*Loc. cit.*

Male, aged twenty-five years. The patient had attacks of abdominal pain a few months previously which were relieved when bowels moved. Three days before admission he had a severe attack of pain after drinking water. His bowels moved freely and he vomited. Bowels had not moved since first day of illness. Abdomen was retracted and rigid, with tenderness in the epigastrium. At operation an intussusception appeared which was nearly gangrenous. It was resected, and ileum was joined to cecum by means of a Murphy button. Patient recovered. At the apex of the intussusception was an inverted Meckel's diverticulum four inches long, gangrenous at the tip.

Case 39.—1913. Drummond, *Surg., Gynec., and Obst.*, 1913, p. 656.

Male, aged thirty-four years. In August, 1911, began to have attacks of abdominal pain with rumbling and sometimes diarrhea. In November, attacks became more pronounced. A week before admission the vomit contained blood. For three days before admission he vomited incessantly and complained of pain coming on in spasms. When examined, pulse was 128; temperature, 98°; abdomen was distended, no intestinal movements visible. Rectal examination was negative. Enterotomy was done and death followed in two days from toxemia. Postmortem examination showed an intussusception with a Meckel's diverticulum three inches long at the apex.

Case 40.—*Loc. cit.*

Male, aged eight years. No record of previous attacks is given. The present attack lasted a week, the intussusception was resected and the patient died. A small Meckel's diverticulum, two inches in length was found inverted into the gut.

Case 41.—1913. Turner, *Guy's Hosp. Rep.*, ix, reported by Wellington, *Surg., Gynec. and Obst.*, 1913, xvi, 74.

Male child, aged sixteen months, operated upon by Lane. There was an intussusception in right iliac region, which was reduced and a second found. This was reduced and a third found. The last contained an inverted diverticulum.

The following cases of intestinal intussusception with an invaginated Meckel's diverticulum are recorded, but insufficient details are given.

Treves, Intestinal Obstruction. Philadelphia, 1884, p. 215. Specimen in Guy's Hospital Museum, No. 1819 (45).

Treves, Intestinal Obstruction, second edition (quoted by Dobson, *Lancet*, 1903, i, 1161). Specimen in Museum of Royal College of Surgeons of England, No. 2718 a.

Adams, *St. Bartholomew's Hospital Reports*, 1891, xxvii, 171. Obscure symptoms of intestinal strangulation had existed about a fortnight. At autopsy an intussusception into the cecum was

found. It contained an inverted diverticulum. Subject was a male.

Willett, *St. Bartholomew's Hospital Reports*, 1891, xxvii, 171. Specimen No. 2183 in the museum of St. Bartholomew's Hospital. Double intussesception of intestine and Meckel's diverticulum in a male.

The following cases are reported as examples of this condition, but are doubtful

O'Conner, *British Med. Jour.*, 1894, ii, 123.

Male, aged thirteen years. Eight days after a severe wetting had two or three rigors, with a temperature of 104°. He was better the next four days, but had no bowel movements, notwithstanding the use of laxative. The next day after the use of opium he passed a portion of the ileum eleven and and one-quarter inches long with a Meckel's diverticulum. "The upper portion was invaginated into the lower, the entire length of the diverticulum appearing through the lower orifice."

Boldt, *New York Med. Record*, 1900, lvii, 655. No details given.

Guyot, reported by Forgue et Riche, "Le Diverticule de Meckel," Paris, 1907, p. 89.

Male, aged ten years. Final attack lasted five days. An entero-anastomosis without resection was done. Death. Autopsy showed an ileocecal intussusception with a Meckel's diverticulum.

Brook, *British Med. Jour.*, 1907, ii, 862.

Taeck, referred to by Von Mondach, *Lancet*, 1907, ii, 1733.

Ryan, *Intercolonial Med. Jour.*, Australia, 1907, xii, 459. Male, aged nine years. Onset of illness acute with pain and vomiting. At operation twelve inches of gut near iliac region were resected. The patient died. The intussusception started from a polyp at the apex.

In summarizing the data of these cases one recognizes regrettable paucity of details, especially as to pathology. A comparative study of the physical condition of the gut, as observed at operation in connection with the subsequent history of the various cases, would be of great value in guiding the surgeon toward the best operative procedure.

Points worthy of special notice are age, sex, manner of onset, appearance of tumor, and the relatively slow course.

Age. The age varied from seven months (29) to 39 years (26), the average in the 41 cases quoted being thirteen years. Of these 20, or 49 per cent., were under ten years of age, 10 between ten and twenty years.

Sex. Of those in which the sex is given 31 were males and 7 females, giving a ratio of over 4 males to 1 female.

Previous Attacks. In 17 of the cases a history of previous attacks is given. In none of the other cases is it specifically stated that there were no previous attacks. In those cases in which previous

attacks have been recorded it stands out so plainly that one is disposed to suspect that some of the reporters may have overlooked the importance of a history of previous trouble in the making of a diagnosis. For this reason it seems worth while to examine these histories with some care. The factors worthy of attention are the number of previous attacks, the location of the pain, the presence of a tumor, and the presence of blood passed per anum. In 3 of the recorded cases (5, 27, and 28), a single attack is mentioned, and this was the case in our patient. In 1 (33) two attacks are mentioned. In 9 (6, 14, 23, 26, 30, 34, 35, 38, and 39) many or repeated attacks are mentioned. In 1 case (21) monthly attacks since the age of two years are mentioned, and in 1 (22) the pain is mentioned as having been present continuously for six months. The character of the pain has been described as dull in 1 case (17), colicky or cramps in 6, 21, 22, and in our own case. In 1 case (14) the pain is recorded as having been in the right side, in 2 (16 and 34) about the navel, and in our case just below the navel. In 1 case (14), in which obstruction was diagnosticated a a tumor was felt and in our case a tumor was diagnosticated during the existence of the obstruction. Blood was discovered in the stool but twice (21 and 27). It is interesting to note that the ages of these two patients were respectively seven and eight years, a later age than the usual occurrence of simple intussusception.

The Final Attack. The history of the final attack which brought the patient to operation or autopsy (or both) presents much that is interesting. In this, too, as in the history of preceding attacks there is a want of negative history, so that it is impossible to determine if certain cardinal symptoms were absent or whether the historian was ignorant of their interest or importance and failed to make record of their presence.

It is a matter of judgment as to what factors shall be considered of fundamental importance. The nature of the disease indicates what factors are likely to be most prominent and likewise what secondary features are likely to appear. Thus pain may be regarded as the cardinal feature; accompanying this are vomiting and distention as positive results of the obstruction and absence of stool and flatus as negative results. Tenderness and rigidity of the abdominal walls and the presence of free fluid in the abdominal cavity give evidence as to the degree to which the intestine has suffered from its acute malnutrition. Conversely, blood in the stool gives similar evidence of the state of nutrition of the mucous membrane. With this general scheme in mind we may proceed to investigate our evidence.

Pain. We may assume that pain is present in every case and our interest lies in its character and location. It is usually colicky in character, and is located usually about or below the umbilicus

or in the right side. The pain bears evidence of the preponderance of traction in the production of symptoms in the condition in question as compared to some other type of obstruction. It is intense, cramp-like, and is disposed to intermission. Usually there are periods of nearly or quite complete freedom from pain. It is not attended by evidence of inflammation and collapse.

Vomiting. In 24 cases this symptom was reported present. In 1 case (18) it is stated to have been present the first thirty-six hours, and in 1 (21) for the first day and in 1 (32) at the beginning. In 1 (27) it is not noted until the eighth day. The character of the vomitus is usually dark green or yellowish. In 1 case (39), the vomit a week before admission contained altered blood. Vomiting, compared to many types of intestinal obstruction, is characterized by its moderate intensity.

Meteorism. The relation of this symptom of vomiting is indicated by the fact that in all but 5 of the 23 cases in which there was vomiting, meteorism likewise is recorded. In 2 of the 3 exceptions meteorism is stated to have been absent, and in the others it is not mentioned. The records on this point are rather striking, inasmuch as in this disease meteorism never appears to be pronounced. Possibly this is because at the time of obstruction distention of the gut seldom reaches a degree comparable to instances in which paralysis is a factor.

Tenderness. This symptom is usually associated with the previously mentioned phenomena of vomiting and distention. It is less often present, however, for in 3 cases it is stated to have been absent, while both tenderness and meteorism were present. In our case tenderness was present but not marked. It is nearly always a late symptom.

Rigidity. In 1 case (15) only is rigidity stated as being board-like, and in 1 (17) the right rectus was stated to have been rigid. In Case 38 the abdomen was rigid and retracted. In our case the right rectus was more rigid than the left, but yet lacked the rigidity of a response to an inflammatory process. On the whole it is a negative sign.

Abdominal Exudation. The presence of a free exudate was noted in 10 and 32 and was well marked in our case. In a number of other cases it is stated that a quantity of fluid escaped when the abdomen was opened, though no note was made of it previously. In these it is more than likely careful examination would have shown free fluid in the flanks. Its value as a sign consists in that if its presence is detected it may mislead the observer to believe that an inflammatory exudate is present.

Blood in the Stool. In 12 it is specifically stated that blood was present in the stool, but in each instance the amount was but slight, except in Case 34 in which a pint of bright blood was passed. In 4 (2, 23, 27, 30,) it is also specifically stated that there was no

blood. The same is true in our case. When blood is present tenesmus is not marked.

Tumor. The most typical factor in the picture of the disease is the presence of tumor. Tumor is stated to have been present in 20 of the recorded cases. In our case the attending physician was able to palpate tumor on the third day, but when the patient came into our hands none could be felt because of the distention. Dulness and resistance were noted in the right flanks of two additional cases (2 and 12). In 2 cases it is specifically stated that no tumor could be felt (2 and 15). In 2 cases (10 and 29) tumor was felt under narcosis. The location of the tumor is interesting. The most frequent location is in the ileocecal region, where 7 were found and next in frequency were 2 in the hepatic region, while 4 were in both these regions, beginning in the ileocecal region and extending to the hepatic region. In 2 cases (3 and 34) the tumor was located below the navel, once (7) in Douglas' pouch, once (22) to the left of the uterus, once (37) felt per rectum, and in our case to the right of the umbilicus. The tumor is sometimes described as sausage-shaped, sometimes movable, and sometimes variable in size and consistency.

Duration of the Disease. The time the disease had existed from the beginning of the illness until it came under observation varied from twenty-four hours (8) to twenty-eight days (10). One was thirty-six hours (6), 2 were forty-eight hours (19 and 34), 7 (13, 28, 29, 30, 31, 37, 38) were three days, 1 (36) was four days, 1 (3) was five days, 2 (15 and 21) six days, 5 (24, 27, 35, 39, 40) seven days, 1 (23) eight days, and our case was five days. This bears evidence that the malady is but moderately acute and accounts for the modified form in which some of the cardinal symptoms of obstruction appear—notably, vomiting and meteorism.

Diagnosis. From the foregoing it is evident that the material out of which to construct a diagnosis has varied in the different cases. It is worth while to summarize this material and to compare it with groups of analogous symptoms produced by other diseases. Pain is the prominent symptom, is usually the earliest to appear, and is the most persistent. The characteristic feature is its cramp-like intermittent character. Its location is usually in the middle of the abdomen, sometimes more to the right side. To pain the evidence of obstruction is soon added, usually vomiting first. This may be early, when it is a reflex from the cramp-like pain or later, when it is the result of the accumulating intestinal contents. In the former case the vomitus may consist of food or greenish mucus, and in the latter of large quantities of yellowish or brownish fluid. With these indications of abdominal storm the lack of abdominal tenderness and muscle rigidity, coupled with a normal or subnormal temperature, marks the condition as some disturbance of the fecal current. The presence of repeated disturbances

leading up to the attack with the above symptoms should give some hint as to the nature of the malady. Our own case had all the ear-marks of the disease and should have been diagnosticated if we had but had the opportunity to study the recorded literature before proceeding to operation.

Differential Diagnosis. This disease may be mistaken for obstruction due to other mechanical causes or to abdominal disasters, mostly inflammatory, which interfere with the dynamics of the intestinal tract in an indirect way.

The causes for obstruction which might come into question are the various internal hernias and strangulations, notably those dependent upon a looping of the gut about a band. These bands may be inflammatory in origin or may be due to congenital anomalies, such as a Meckel's diverticulum attached at both ends. Some of the internal fossæ may ensnare a loop and give rise to similar symptoms. Furthermore, these conditions may give a history of repeated attacks almost like those of intussusception. The presence of a tumor, however, will exclude the probability of band obstruction and to a less degree that of fossa obstruction. Intussusception without diverticulum usually occurs in the first year and a half of life, so that in these cases one can assume the presence of a Meckel's diverticulum only when there is a hard nodule at the head of the intussusception or some deformity at the umbilicus. It is presumed that any surgeon sufficiently advanced in his profession to have any acquaintance with the literature of intestinal obstruction would not fail to exclude hernia of the external openings.

The inflammatory lesions of the abdomen usually present symptoms plainly divergent from those of the affection under discussion, yet because of their frequency they are likely always to be present in the surgeon's mind. Perforative lesions are regularly attended by sudden pain, but it is not cramp-like and remissions are not apt to intervene. The practitioner, to be sure, may cause perforation to simulate intussusception by giving morphin, and may thus confuse the surgeon. Tenderness and rigidity also in this way may be suppressed, but it is not usual for an abdomen which is the site of an inflammation severe enough to demand large doses of morphin to quiet down under its influence sufficiently to obliterate all evidence of tenderness and resistance. The general appearance of the patient may give evidence of a severe inflammatory lesion in the belly, and even if the distinctive symptoms are neutralized by morphin, an expert clinican should be able to read the patient's true condition in his face. As in all cases of obstruction the absence of reactive manifestations is a most important differential point. The absence of accelerated pulse rate and the normal or subnormal temperature are very suggestive. In this respect, however, fallacies beset the diagnosis from two directions. Other abdominal lesions such as perforative appendicitis may show little

or no reaction, and in the late stage of the disease under discussion the pulse may be rapid and the temperature may rise.

The diagnosis in complicated cases is thus not to be made upon general evidence, but upon the consideration of the special features of individual cases. If the disease has been determined to be surgical it is important to decide between an obstruction and an inflammatory lesion, for upon this decision depends the position of the incision. That this is not always easy is shown by the late hour at which so many cases reach a final solution, often indeed at autopsy. Lesions not surgical in character, which are capable of giving a like series of symptoms, are numerous. The early age of most of these patients excludes the two diseases, aside from frank inflammatory conditions, which most resemble obstruction—namely, gall-stones and pancreatic disease. The ephemeral nature of the acute intestinal colics should differentiate them at an earlier date than has been done in most of the reported cases. The fact that some of the cases of the disease under discussion had been preceded by a series of slighter attacks naturally leads to delay in the hopeof the same favorable outcome. That blood in the stool should be ascribed to dysenteric diseases is excusable, since in this affection the pains are often diffuse over the abdomen. In dysentery the passage of mucus and stool is accompanied by tenesmus, but in intussusception blood passes without tenesmus unless the inverted gut approaches the anus in which event it may be reached by the palpating finger. After tumors appear or meteorism gradually ensues delay should not be countenanced.

Pathogenesis. The factors responsible for the invagination of Meckel's diverticulum have been the subject of much speculation. The one essential is that the distal extremity of the diverticulum be unattached. It has long been known that the floating diverticulum is subject to a varity of accidents, of which torsion has been the most common. The blood supply being derived from the small intestine usually opposite its own source of supply makes the nutrition of the diverticulum at all times somewhat precarious. That gangrene about the base should occur need therefore occasion no surprise.[1] To what degree such accidents may be responsible for the various narrowings and thickenings at the attachment of the diverticulum and of the intestine itself is open to question. Gray (24) believes that such accidents are responsible for their existence. Careful histologic study which might throw some light on the subject is lacking. That some of these anomalies are congenital is quite likely. Even though it is granted that they are the result of pathologic processes, the mechanics of inversion is not explained. Küttner[2] was of the opinion that in his case of inversion of the diverticulum an accessory pancreas at the tip of

[1] Gray, British Med. Jour., 1907, ii, 825.
[2] Beitr. z. klin. Chir., 1898, xxi, 289.

the diverticulum was responsible. He thinks that a polypus or a fecal mass might act in the same way. Accessory pancreases were present in Brunner's (8) case and in one of Drummond's (35), and a small lipoma was present in Zum Busch's. In Moroni's case (5) the diverticulum contained a fibrous polyp. Gray believes the presence of such a tumor would prevent rather than assist in the production of inversion. De Quervain (2) believed the rush of fluid along the intestine produced a negative pressure sufficient to produce an invagination. Gray (27) believes invagination begins at the base of the diverticulum, congestion at this point as the result of torsion causing swelling and mucus production being, according to him, the fundamental factor. That the mucosa is loosely attached is proved by Hohlbeck's (10) case in which the mucosa alone was invaginated. A narrowed base would permit an accumulation of contents, which when forced by active peristalsis into the lumen of the gut, might easily be accompanied by mucosa and this would ultimately drag the musculature after it. Intussusception might then follow immediately or sometime later.

The study of our case and of the literature would lead us to believe that intussusception of the gut at the point of attachment of the diverticulum is the first event and that inversion of the diverticulum occurs as a secondary process. A thickening of the gut wall at the site of attachment of the diverticulum might readily give the stimulus to such a course of events. That such an event is mechanically possible is illustrated by a case recently reported by Kasemeyer,[3] in which a carcinoma of the cecum became the apex of an intussusception. Other like instances have been reported. When a foreign body is to be propelled along the intestine this is accomplished by a relaxation of the wall in front of the object and a contraction behind it. If the thickening in the intestinal wall project within the lumen the physical characteristics of a foreign body within the intestine are produced. Such a thickening may occur within the diverticulum leading to a primary inversion of the diverticulum or it may occur about the base of the diverticulum in the wall of the intestine proper leading to an intussusception without an inversion of the diverticulum. It is only by such a mechanism that an inversion without intussusception or an intussusception without inversion can be explained. There must be a course common to them both. That such changes do occur is demonstrated by our case. Partial inversions or beginning intussusception would explain the repeated slighter attacks.

Treatment. Obviously treatment must be surgical. Enemas can hardly find a justification at the present time. The ideal procedure is reduction of the intussusception and eversion of the invaginated diverticulum, to be followed by the resection of the

[3] Deutsch. Zeitschr. f. Chir., 1912, cxviii, 205.

diverticulum. In order that this may be carried out the gut in all its portions must retain its integrity so as to permit the necessary manipulation, and the circulation must be in such a state as to maintain the nutrition of the gut after the treatment is completed. The invagination may be irreducible or the gut when relieved of its intussusception may not be viable. These possibilities must be judged at the time of the operation, for the state of the gut is dependent upon the duration and the degree of constriction to which it has been subjected. The former factor only is known in a given case. The treatment is divisible, therefore, under the following heads. (1) "When the gut is reducible and viable," and (2) "when irreducible or reducible and not viable."

When Reduction is Possible. In these instances the reduction of the intussuscepted gut is attempted by gentle pressure from above with the guarded assistance of traction from below. In some instances it has been easily accomplished, as in Cases 7, 8, 9, 10, 17, 19, 20, 22, 24, 26, 29, 31, 34, 35, and 41; while in Case 14 some difficulty was experienced. This may be said of our case. In Case 33 reduction was accomplished with difficulty. The diverticulum was reduced in Cases 19, 20, 24, 26, 38, and our own case. In none in which the intussusception was easily reduced was resection necessary except in Case 17, which was reduced easily and then resected, and in Case 29, in which the bowel was torn by the manipulation. It would seem therefore that if the gut is easily reducible it will be in such a condition that resection will not be required. In 1 case, however, (33) reduction was possible, yet gangrene occurred, requiring a secondary resection.

When the gut is reducible the problem of viability must be decided. The problem here is no different from that in any other case of intestinal obstruction. If the gut is in active peristalsis, after being rereleased, it is viable. Slight peristalsis, according to Gaardlund[4] may occur in a gut which subsequently becomes gangrenous. Mesenteric thrombosis and great edema of the gut wall indicate impending gangrene. A deep lusterless black indicates necrosis. Less degrees of discoloration are compatible with restitution and one or more of the usual means for determining the point may be employed. These are chiefly the temporary use of warm compresses, the temporary exclusion of the suspicious loop without the abdominal cavity, and provision for drainage about the replaced loop, with the hope that should integrity fail external drainage will rescue the patient.

Gaardlund,[5] in a very carefully studied case, has called attention to the fact that the mucosa may be injured beyond repair when the musculature is still apparently viable. This is capable of producing delayed disaster. Reports of fatal cases are not full

[4] Arch. f. klin. Chir., 1912, xcviii, 433. [5] Loc. cit.

enough to permit a judgment as to whether or not a too conservative procedure has been responsible for deaths. Information as to the state of the mucosa in fatal cases in all types of obstruction is much desired.

When the Gut is Irreducible. Resection obviously must be practised if reduction is not possible or if injury is inflicted upon the gut in the process of reduction. Thus in Cases 1, 2, 3, 4, 6, 11, 13, 15, 17, 18, 21, 23, 25, 29, 30, 32, 36, 37, 38, and 40 resection was done. When the gut is irreducible or if reducible, obviously unviable from gangrene or thrombosis already present or inevitable from injury to the mesentery or the gut wall inflicted during the effort at manipulation, a solution of continuity of the intestinal circulation is unavoidable. Three plans are open to the operator. (1) An artificial anus may be made prŏximal to the point of obstruction, allowing for the removal of the irreducible mass and the reëstablishment of the intestinal canal at a future date, or (2) the mass may be resected and the free ends of the gut brought externally, either with or without the employment of Paul's tubes, leaving the establishment of the gut continuity to a subsequent date, or (3) the mass may be resected at once and an anastomosis made.

In solving problems of treatment one must be guided by the experience of one's self and of others in the same class of cases and in allied cases which present analogous features. The personal equation of the operator here will have free play.

Reasoning from analogy it would seem that if the novice should meet such a problem an artificial opening would afford the patient the best chance of life. The same is true in the hands of the more expert when working under exceptionally unfavorable conditions. In other conditions resection of the offending mass should be done. Immediate anastomosis may or may not be done depending on the condition of the patient's intestinal tract. If the patient is still possessed of good power of peristalsis a skilful operator may proceed at once to anastomosis. If the gut has little or no visible power of propelling its contents, anastomosis would better be deferred. Unquestionably the stagnating intestinal contents will flow out of a Paul's tube with greater facility than through a new anastomosis opening and will be much sooner beyond the reach of avenues of absorption. Greater moral courage is required to quit than to go on.

If we try to substantiate these views from the recorded histories we are met by the fact that operators, except in a few cases, have chosen to do an immediate anastomosis, a fact which one could divine from reading the outcome of these cases.

Of the resected cases in which definite information is available 13 died and 9 recovered, which represents a high mortality; 5 of these cases came to operation in six to eight days, indicating a subacute process and one on the second (17), 5 on the third (13,

28, 30, 37, and 38) day and one (36) on the fourth day. One in which drainage was done (12) recovered and 1 (39) died. Of those in which reduction was possible, necessitating the removal of the diverticulum only, 9 recovered and 4 died. The better operative prognosis in the cases in which injury to the gut is slight is obvious.

The cause of death in those where reduction was possible and resection was not done remains to be determined. In Gaardlund's case reduction was possible, but secondary gangrene took place and he saved the patient by a secondary operation.

For the reduction of the mortality one must apparently look in the direction of a closer study of the advisability of resection when the gut is reducible or the question of drainage and temporary resection where the gut is certainly lost. More radical procedure in some of the simpler cases and more conserative procedure in the very grave cases seem to be the lines along which we may hope to advance to a better prognosis.

SPINAL GLIOSIS OCCURRING IN THREE MEMBERS OF THE SAME FAMILY, SUGGESTING A FAMILIAL TYPE.[1]

By George E. Price, M.D.,

ASSOCIATE PROFESSOR OF MENTAL AND NERVOUS DISEASES, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA, PA.

The following cases present not only an unusual symptom group, but are chiefly of interest owing to the development of the condition in three members of one family, two brothers and a sister. One of the cases, C. S., a boy, aged thirteen years, came under my observation in May, 1912, following his admission to the neurological service at the Jefferson Hospital. The other cases, P. S., female, aged twenty-four years and E. S., male, aged twenty-two years, were studied in November of the same year. As the symptoms were practically identical in all three patients, one, the eldest, will be recorded in detail as illustrating the condition:

P. S., female, aged twenty-four years, single. She had the usual diseases of infancy and childhood and an attack of influenza when sixteen. Her menses began at the age of sixteen years and were regular and not especially painful. When she was aged about eight years a small sore appeared on the second toe of her right foot; her mother, thinking the sore contained a splinter, opened it and removed a small spicule of bone, the wound subsequently healing rapidly. Two years later a similar condition developed on the

[1] The cases were presented before the Philadelphia Neurological Society, November 22, 1912.

second finger of the right hand. The patient states that she does not remember ever having been able to button her clothing at the back, nor has she been able properly to recognize touch, pain, heat, or cold on her hands and feet, but can recognize these sensations readily on other parts of her body. That all forms of sensation were lost in the affected areas was elucidated in the physical examination.

FIG. 1.—Hands of C. S., showing clubbing of fingers and trophic changes of nails.

EXAMINATION.—The fingers of both hands show marked trophic changes, some being affected to a greater degree than others. The fingers most involved show spontaneous amputation of the distal phalanges, either partial or total. The ends of the fingers are clubbed, and where the nail remains it is thickened, and presents marked transverse ridges. The skin over the hands is markedly thickened. All of the joints of the fingers are enlarged and stiff, the second joint of the middle finger, right hand, showing the most distinct arthropathy. The right foot is clubbed; the great toe is absent and the second toe partially gone; the other toes are deformed and displaced upward and backward. The foot is reddened and macerated, showing an inflammatory condition, due to a secondary infection, with some swelling and edema of the ankle and leg.

The left foot shows loss of the little toe and partial loss of the other toes; a scar on the inner side of the base of the great toe indicates the site of extrusion of a spicule of bone. The joints of the toes of both feet present changes similar to those described as occurring in the finger joints.

All forms of sensation are entirely lost over both hands; from wrists to elbows, sensation is preserved but diminished; from elbows to shoulders, sensation is slightly diminished. In the lower extremities all forms of sensation are lost over the feet, ankles, and lower third of both legs; from this point to just above the knees sensation is preserved, although diminished, and then is but slightly diminished to the hips. Over face, neck, and trunk sensation is normal.

FIG. 2.—Hands of E. S., showing loss of terminal phalanges and enlargement of joints.

The gait is halting, owing to the inflamed and deformed foot, but is otherwise normal as is also the station. There is no muscular wasting, and the patient presents no tremors, palsies, contractures, nor spasticity. There is no scoliosis. The reflexes of the upper and lower extremities are all absent. Babinski's sign is absent; neither is there ankle clonus. The nerves and bloodvessels of the extremities present no gross abnormalities. Mentality is normal.

One of the cases, C. S., presented in addition to the changes described above, superficial ulcers, varying in size from a quarter to a half dollar, over both lower extremities from ankles to knees, chiefly over the anterior border of the tibiæ, also a couple of smaller ulcers over the insteps. These were trophic in character, and the result of trivial contusions, as the boy was very active physically.

Eye examinations were made by Drs. Le Fever and Shannon, and proved to be negative except in the case of E. S., who had concomitant squint (functional) of the right eye.

FIG. 3.—Legs and feet of C. S., showing superficial trophic ulders, etc.

Urinalyses were negative in all three cases, and the blood findings were normal except for a slight diminution in the number of erythrocytes and relative decrease in the amount of hemoglobin, which were not sufficient to be of any pathological significance.

A Wassermann test in each case was negative.

An *x*-ray examination of the right foot of P. S. and the right hand of E. S. was made by Dr. Manges, which revealed trophic changes in all of the bones of the foot except the os calcis, astragalus, and scaphoid. The terminal phalanges of the hand were similarly affected.

FIG. 4.—Feet of P. S., showing ulceration, loss of terminal phalanges, secondary infection, etc.

Investigation of the family history failed to disclose any possible etiological factor. The father and mother were living and well, having beside the three affected children, two other children, aged five and six years respectively, in perfect health. There was no history of nervous or mental disease, alcholism, tuberculosis, or consanguinity in the family. It should be noted that the two healthy children have not reached the age at which the symptoms first appeared in their sister and brothers.

The system-complex presented by the above cases is comparable to the condition described by Morvan in 1833 as occurring among the fishermen in Brittany. Joffroy and Achard, Thomas, and others have since demonstrated central-cord cavities in this affection and a peripheral neuritis has also been observed by Joffroy and Achard and by Gombault. These findings have led to Morvan's disease being considered as a form of spinal gliosis associated with peripheral neuritis. Bernhardt and Jolly many years ago called attention to the absence of any fundamental difference between Morvan's disease and syringomyelia. Gowers in discussing the

nerve changes in this affection says that we must consider whether these changes are of developmental origin, and adds, "It is quite possible that they may share the condition of arrested development, entailing a liability to later morbid changes."

In considering the diagnosis, Raynaud's disease was excluded by the absence of the characteristic vasomotor changes and the presence of whitlows with the loss of sensibility. In sclerodactyla there would be no loss of sensation nor spontaneous amputation of fingers and toes.

Anesthetic leprosy was also considered, but cutaneous pigmentation was absent and the sensory disturbance was segmental instead of corresponding to peripheral-nerve distribution. In confirmation of this, Drs. Stelwagon and Gaskill, of the dermatological department of the Jefferson College, examined the cases and reported that the lesions were not those of leprosy.

The writer has been unable to find any instance of the syndrome occurring in two or more members of one family, and considers that the marked familial tendency exhibited in the above cases suggests the possibility of a new familial type.

THE TECHNIQUE OF ABDERHALDEN'S PREGNANCY REACTION.[1]

By Charles C. W. Judd, A.B., M.D.

(From the Laboratory of Clinical Pathology and Experimental Medicine, College of Physicians and Surgeons, Baltimore, Maryland.)

Abderhalden,[2] through his studies into the manner in which the animal body protects itself against alien material which gains access into the blood stream, has evolved the theory that the blood plasma, when the tissues are stimulated by the invasion of such foreign substances, acquires enzymatic properties which do not normally exist; that the enzymes so produced act as protective agents by splitting the complex and harmful antigenic carbohydrate, fat, or protein molecule to assimilable cleavage products of the same, as occurs normally in the gastro-intestinal tract; that these enzymes are specific in character for their particular antigenic molecule; that the action of such ferments may be studied extracorporeally; and finally, that their presence may be demonstrated by physical and chemical means.

He has recently applied[3] these discoveries in the demonstration

[1] The observations upon which this contribution is based were completed April 1, 1913.

[2] Schutzfermente des tierschen Organismus, J. Springer, Berlin, 1912.

[3] Münch. med. Woch., lix, No. 24; ibid., lix, No. 36; Deutsch. med. Woch., xxxviii, No. 46.

of the specific proteolytic enzyme induced by placental tissue as a means of diagnosticating pregnancy. The extracorporeal demonstration of such a specific enzyme is effected by bringing together some blood serum of the suspected subject and prepared placental tissue derived from the same or a closely allied species. If the enzyme is present, cleavage of the placental protein content takes place under favorable conditions; if absent, no such cleavage occurs under analogous circumstances. If the enzyme is present, the subject is considered pregnant; if absent, non-pregnant. The presence or absence of cleavage of the placental protein content is detected in either one of two ways: (1) By accurate polariscopic readings of the suspected serum in the presence of prepared placental tissue, both before and after a period of incubation of these two substances. The readings are identical in the absence of cleavage, whereas a change in the degree of rotation indicates splitting of the protein molecule. This method requires a very accurate and expensive polariscope. (2) The second method for the detection of cleavage employs a semipermeable dialyzer whose pores are sufficiently large to admit of diffusion on the part of the cleavage products of the placental protein, but impermeable to the intact placental protein molecule. Prepared placental tissue and a portion of the suspected serum are placed in a dialyzer. After a period of incubation the cleavage products are tested for in the dialysate by means of the biuret reaction or a modification of the same.[4] If the characteristic color reaction is obtained, cleavage and dialysis of the cleavage products have taken place, while no visible chemical reaction indicates the absence of cleavage.

Though my cases so far are too few (thirty to thirty-five, including control cases) from which to draw any definite conclusions, there are certain details in the technique upon which little if any stress has been laid which have manifested themselves as being most essential to obtaining reliable results. Moreover, there are some features which, even more than the original procedure,[5] place the method in the hands of those without a well-equipped laboratory. For these reasons it has been thought advisable to bring them to the attention of others at this stage of the investigation, rather than delaying until the conclusion of the series.

Foremost among the tendencies to vitiate results are putrefactive changes, which artificially split the placental protein to dialyzable decomposition products yielding a positive biuret reaction. A few drops of toluol, as suggested by Abderhalden, added to the dialyzer and to its container at the beginning of incubation have been found insufficient to invariably prevent

[4] Abderhalden advocates the use of tri-keto-hydrindenhydrate (marketed by Farbwerke-Hoechst Co. as "Ninhydrin," from the Japanese, meaning pregnancy). This reagent has been the one of choice in this series.

[5] For this procedure the reader is referred to Abderhalden's own articles, already cited.

putrefaction, particularly at 37° C., when that amount of preservative soon evaporates, leaving the tissue, serum, dialyzer, and dialysate unprotected from invading microörganisms. A generous layer of toluol to both the contents of the dialyzer and its container has gone far to correct this error.

Again, the method of storing the dialyzers as suggested by Abderhalden proved but a means of allowing them to become a nidus for putrefactive bacteria when any attempt was made to use them for more than a single test. If, however, after each experiment the following method is employed, dialyzers may be repeatedly, though not indefinitely, used for subsequent examinations. Thoroughly cleanse dialyzer and container after each test in tap water, allowing both to soak in the same for a few hours, to remove all traces of protein from the surface and pores of the dialyzer. Place the dialyzer in the container and submerge the former in distilled water. Plug the mouth of the container with cotton and sterilize the whole in an autoclave or steam sterilizer, after which the entire apparatus may be conveniently stored, awaiting future use, when, except for pouring off the excess of distilled water, it is ready for another experiment. It has been found that this has been a considerable saving of both time and material, while putrefactive errors have been greatly reduced.

A third precaution against putrefactive error early suggested itself, that is, the possible putrefaction of the stock of placental tissue. It may be overcome by the use of either of two controls for each set of tests made. The supernatant water of the stock placental preparation may be tested for the biuret reaction each day tests are to be made. If suggestively or definitely positive, treat the tissue as though freshly ground placenta, boiling with changes of water until the biuret reaction has entirely disappeared. If putrefactive changes are marked, the entire preparation should be discarded. The same error can also be detected by incubating a portion of the tissue in the presence of sterile saline solution instead of serum in a control dialyzer, testing the dialysate at the end of incubation for the biuret reaction. Either of these simple controls not only prevents a possible error in the result of the test, but also materially increases the longevity of one's placental preparation. One at hand is perfectly serviceable after four months have elapsed since it was first prepared.

Finally, on the ground of putrefactive vices the serum for the tests should be collected and handled throughout with at least an approximately aseptic technique.

An error of different origin, of which no mention in the literature has been observed, at least specifically, is that relative to the variations encountered in the permeability of the dialyzers. Schleicher and Schüll's Diffusions-Hülsen, No. 579, the ones recommended as most applicable for the purpose in hand, are in my experience

not proof against disastrous errors, unless certain precautions are exercised. In the first instance, not all such dialyzers are impermeable to normal serum, which, passing through into the dialysate, imparts to it a biuret reaction. To eliminate this error each dialyzer should be subjected to a preliminary "try out," with either blood serum or a serous effusion. All those permeable to such material should be summarily discarded. The period of incubation for this "try out" should obviously be the maximum—sixteen to twenty-four hours at 37° C.

The reverse of this fallacy, the non-permeability of the dialyzers to proteoses and peptones which roughly correspond to the cleavage products of the complex placental protein, is not only conceivable but has been encountered in many of the second "try outs," with an aqueous solution of Witte's peptone, which has invariably preceded the use of all dialyzers employed in this test. The period of incubation for this determination should not exceed the minimum time—twelve hours.

A further control of the permeability of the dialyzers is recognized in the literature. This consists of testing a portion of each individual serum used in a pregnancy experiment to determine if the selected dialyzers are permeable to that particular serum. It is noteworthy that since the adoption of the preliminary "try outs" already outlined, but one serum has been encountered which has permeated the selected dialyzers. On the other hand, before the preliminary "try outs," when all dialyzers were accepted as suitable, so bizarre a result as a positive test and negative control accompanying it occurred in an experiment with my own serum.

Due to a gradual increase in the permeability of the dialyzers, occasioned doubtless by their repeated subjection to heat, it has been found advisable to ascertain their continued impermeability to serum, after about every tenth sterilization, or the dialyzers may be discarded irrespective of their possible future value after the tenth sterilization.

The real danger of an erroneous diagnosis through the failure of observing these precautions makes of them essential controls in the performance of the reaction.

The inherent faults encountered in the dialyzers recommended led to a trial with home-made celloidin ones. About 6 c.c. of oil-free celloidin were poured into glass cylinders about 10 cm. high and 3 cm. in diameter. The entire inner surface of the cylinders was coated with this as evenly as possible, by rotating and inverting the cylinders, so long as the celloidin remained plastic. When no longer plastic, the celloidin was allowed to set quite firmly, thus forming a hollow cast of the glass cylinder. The upper margin of the cast was then cut around its entire circumference about 2 cm. below the rim of the mould. The lateral walls of the sack were then gently freed from the investing cylinder and gently

removed from it. The separation of the mould from the cast as the process advances is facilitated by keeping the dead space between them filled with water.

Though none of the dialyzers so obtained were impermeable to proteoses and peptones, about the same proportion were permeable to serum albumin as the parchment ones. They have the marked disadvantage of standing sterilization by heat very poorly and appear to be reliable for but the necessary "try outs" and one or, at most, two tests. The apparatus, however, does serve perfectly well when the recommended dialyzers are not available.

The dialyzers submerged in water and placed in their container as before may be adequately sterilized by boiling them for twenty minutes in a covered stew-pan instead of using an autoclave or steam sterilizer.

Any good water free from organic matter may safely be substituted for distilled water.

The necessity of incubating specimens at a constant temperature of 37° C. or therabout for from sixteen to twenty-four hours would require a thermostat for the performance of this test, but it was found that the temperature of a warm room gave about as pronounced a reaction as controls kept in the thermostat, provided that the incubation time of the former was increased to about thirty hours.

As containers for the dialyzers urinometer cylinders or those used in the making of the celloidin sacks serve capitally.

A few controls with a 0.25 per cent. copper sulphate solution demonstrated that all but the slightest degree of dialysis is detected by the biuret reaction as well as by the employment of "Ninhydrin." A greater accuracy in observation is, however, required for the former.

The collection of blood should be by venipuncture. Though the use of a MacRea or Keidel tube is very convenient, a hypodermic syringe of sufficient capacity (6 to 8 c.c.) or even a large hypodermic needle and a sterile test-tube answers all necessary requirements, asepsis and the procuring of hemoglobin-free serum.

Though the foregoing simplifications are not ones of choice, they bring the test within the reach of those not engaged in laboratory practice on a large scale.

My first applications of this serum test for pregnancy were most disheartening, the laboratory findings and the clinical diagnosis being at variance most of the time. The adoption of the foregoing precautions has, however, yielded equally gratifying results. The cases examined, though not many, have covered a considerable range of ground, being positive as early as the seventh week of gestation and constantly so from then on to well into the puerperium. The time of the disappearance of the reaction after delivery has been between the seventh and twentieth day of the

puerperium in those cases in which this point has been investigated. Girls of fifteen and women of thirty-five when pregnant have yielded positive results irrespective of the number of children born. In two cases, one pregnant and the other non-pregnant, in which the laboratory and clinical diagnoses were at variance, the subsequent course of events has justified the former. Both white and colored women have yielded positive and negative reactions in accordance with whether they were pregnant or not. An eclamptic in the sixth month gave a weak but definitely positive reaction. As controls, healthy men, virgins, women past the menopause, and non-pregnant women in the child-bearing period have uniformly given negative results. Likewise many pathologic conditions—syphilis, including one case of tabes, tuberculosis, malignant growths (one a case of carcinoma of the cervix), all acute infections encountered, comprising typhoid fever, general septicemia, acute endocarditis, acute pericarditis, gonorrheal arthritis, phlebitis, and acute pelvic inflammatory disease—these at least have been uniformly negative.

Only by the observance of the added precautions here indicated has the as yet incomplete series of cases undertaken in this laboratory been confirmatory as to the reliability of the serum diagnosis of Abderhalden. On the other hand, with the exercise of these controls the most meagre equipment indicated here has been reliable in the accurate performance of the test, the results being in perfect accord with those reported by Abderhalden.

SEVEN CASES OF CERVICAL RIB, ONE SIMULATING ANEURYSM.[1]

By N. Gilbert Seymour, A.B., M.D.,

ATTENDING PHYSICIAN TO GOUVERNEUR HOSPITAL TUBERCULOSIS CLINIC AND TO ST. GEORGE'S CHURCH TUBERCULOSIS CLASS, NEW YORK.

Of the 7 cases of cervical rib here presented, 5 came under my observation at the Gouverneur Tuberculosis Clinic, 1 at St. George's Tuberculosis Class, and 1 is reported through the courtesy of another physician whose patient she is. In 6 of the cases the condition was discovered in the course of routine chest examination, no attention having been drawn to it by the symptoms recorded; the history of the seventh case suggests the diagnosis.

After the comprehensive articles on cervical rib published by

[1] Five of these cases were reported before the New York Society of Internal Medicine, April 26, 1911. The remaining two were subsequently admitted to my service at the Gouverneur Clinic.

Keen[2] in 1907 and Goodhart[3] in 1909, it is needless to review the previous literature for a *resume* of the subject. In brief, it may be stated that cervical rib is a congenital anomaly which may be associated with other defects of development, chiefly of the central nervous system; or it may exist alone, the latter being usually the case. It is often attended with slight or no symptoms, and may then be discovered only in the course of systematic physical examination, by the *x*-rays or at postmortem. It is often found in conjunction with a scoliosis, usually of the cervicodorsal type, and it is not infrequently associated with a neuropathic diathesis. It is a much more common condition than was formerly supposed, a large number of cases having been reported during the past fifteen years, after attention had been drawn to the subject, and especially since radiography has been available for diagnosis.

Although the existence or possibility of this condition was known to early authors, the first paper published on the subject was that of Hunauld,[4] which appeared in 1742. In 1869 Gruber[5] published a compilation of the recorded cases; but in 1875, one hundred and thirty-three years after Hunauld's description of cervical rib, only 79 cases had been reported, and of these only 5 were recognized during life. In 1894 the number of reported cases had increased to 139, of which 9 were diagnosticated in the living subject.[6] In 1904, 34 cases recognized during life had been reported, and many more discovered at autopsy or in the dissecting room. Since that date a large number of living cases have been reported, in nearly all of which the diagnosis was confirmed by *x*-rays. Up to the publication of Keen's article 43 of these cases had come to operation, and the surgical importance of the condition is there fully discussed.

Although cervical rib is congenital, the age at which it has been discovered ranges from intra-uterine life to advanced years. It is much more frequently found in females than in males, the proportion being variously stated as two or three to one. In about two-thirds of the cases the condition is bilateral. Single cervical ribs are about equally frequent on the two sides. The anomalous ribs usually develop from the seventh cervical vertebra, more rarely from the sixth, and in only one known case from the fifth. Two cases have been reported in which there were two supernumerary ribs on one side.[7]

[2] Amer. Jour. Med. Sci., 1907, cxxxiii, 173.

[3] Ibid., cxxxviii, 666.

[4] Mém. math. et phys. d. l'acad. r. d. sc., lvii, 1742.

[5] Ueber die Halsrippen des Mensch, St. Petersburg, 1869, Mém. de l'acad. imp. d. sci., vii, Series 13, No. 2.

[6] Pilling, Inaugural Dissertation, Rostock, 1894.

[7] "In certain rare cases, accessory ribs have been observed in the lumbar region, but this anomaly is without clinical significance. There is no case on record in which a supernumerary rib had developed in both lumbar and cervical regions in the same individual." Goodhart, loc. cit.

The cervical ribs vary in length from a slight increase of the costal process of the vertebra to a complete rib united at its anterior extremity with the cartilage of the first dorsal rib. They may be flail-like,[8] articulated, or immovable. The symptoms, when present, referable to the existence of cervical rib are of three groups—vasomotor, sensory, and muscular—and are due to the pressure of the bony tumor in the neck upon the subclavian artery and brachial plexus.

The principal vasomotor symptoms noted are visible pulsation of the subclavian artery, variations in the radial, brachial, or axillary pulses, gangrene of the fingers (rare), and edema, which is also rare, as the vein is seldom compressed. Sensory symptoms consist of pain, paresthesias, and disturbances of the tactile and temperature sense. Muscular symptoms of nerve origin include paresis, ataxia, and atrophy.

Actual paralysis has not been observed.

Two points of peculiar interest brought out in the literature of cervical rib are its frequent association with scoliosis and the late development of symptoms referable to the supernumerary rib. This latter fact has been variously attributed to growth of the individual, to trauma, to loss of flesh as a result of constitutional diseases, to arteriosclerosis, and to the retraction of the pulmonary apices in healed tuberculous lesions.

In all of the following 7 cases the cervical ribs were bilateral. In Case II, the supernumerary rib was apparently on the right side only, and in Case III on the left, but in both instances the *x*-rays revealed an undetected rib on the opposite side. In Cases VI and VII, both cervical ribs were rudimentary. In but 2 cases were any pressure symptoms reported, in both instances sensory, none showed any of the vasomotor phenomena, and but 1 the neuromuscular symptoms, described above. Six of the 7 cases were females.

The *x*-ray examinations of these patients were made by Dr. William H. Stewart, radiographer to Harlem and Gouverneur Hospitals, to whom I am also indebted for the plates and descriptions illustrating Cases II and III. I wish to make acknowledgment also of the courtesy of Dr. Henry E. Wise, in supplying the prints which accompany Case VI.

Case I.—R. E., female, now aged twenty years; married; born in the United States. Her family history was negative. The previous medical history was not significant. She gave a history of influenza three times. It was shortly after her first attack, five years before, that she was sent to the Gouverneur Tuberculosis Clinic for examination. At that time she was pale, undernourished, and had a slight cough. She had no symptoms suggesting cervical

[8] Francine, Amer. Jour. Med. Sci., 1910, cxxxix, 108.

rib, but examination revealed prominent supraclavicular spaces on both sides, which on palpation seemed to be due to the presence of small bony masses near the cervical end of the fossæ. The percussion note over these masses was dull, and the breath sounds at the apices were distant, leading at first to the suspicion of tuberculous infiltration. The *x*-rays revealed the presence of double cervical ribs. The chest was otherwise negative, and the case was dismissed later as non-tuberculous.[9] Now, after an interval of five years, the patient reports herself in good health. Since her discharge from the clinic she has married and has one child. Recently, however, there have developed some slight symptoms referable to the anomalous ribs. There is some impairment of the circulation in the right hand after prolonged use, manifested by a sensation of slight numbness, but without changes in color and without edema. She also complains of occasional pain "on top of the left shoulder."

The chief point of interest in this case is the presence of two well-marked cervical ribs occurring without symptoms of any kind until the patient reached the age of twenty, but giving rise to physical signs at the apices which suggested pulmonary tuberculosis.

Case II.—A. K., female, aged sixteen years; Russian; occupation, milliner's trimmer. Her family history was negative. She had a personal history of measles and muscular rheumatism. About one year ago, she complained of slight cough and progressive weakness. She had been well previously, though overworked and living under unhygienic conditions. Several months after the beginning of her illness she was obliged to stop work because of weakness and dyspnea, and about this time she applied to the Central Health Department Tuberculosis Clinic for examination and treatment. She was there under observation for a time, and was discharged as not tuberculous. In July, 1910, she was sent into Gouverneur Clinic for examination through the courtesy of Dr. Charlotte Blum of the clinic staff, with the diagnosis of chronic endocarditis and aneurysm of the right common carotid artery. Physical examination revealed a small pulsating tumor, well above the inner end of the right clavicle. Percussion was flat over this mass and impaired at the outer end of the supraclavicular space. A distinct thrill and pulsation, which seemed to be expansile, could be detected on palpation, and on auscultation there was a loud systolic murmur synchronous with the apex beat and radial pulse. There was little if any difference between the right and left radial pulse. On deep palpation the pulsating tumor seemed to be superimposed upon a hard immovable mass of bony

[9] This case, illustrated by *x*-ray plates taken at Hudson Street Hospital, was shown at the Practitioners' Society April 6, 1906, by Dr. Lewis A. Conner, and reported in the proceedings of the Society, Medical Record, lxix, 19.

consistency, which could be traced backward to the spine. Further examination of the chest revealed the characteristic signs of chronic endocarditis (mitral regurgitation), in a stage of incomplete compensation, to which could be attributed the dyspnea, cough, and weakness of which the patient complained. The lungs were negative. The patient was sent into the wards of Gouverneur Hospital, with a diagnosis of endocarditis and of right cervical rib with the

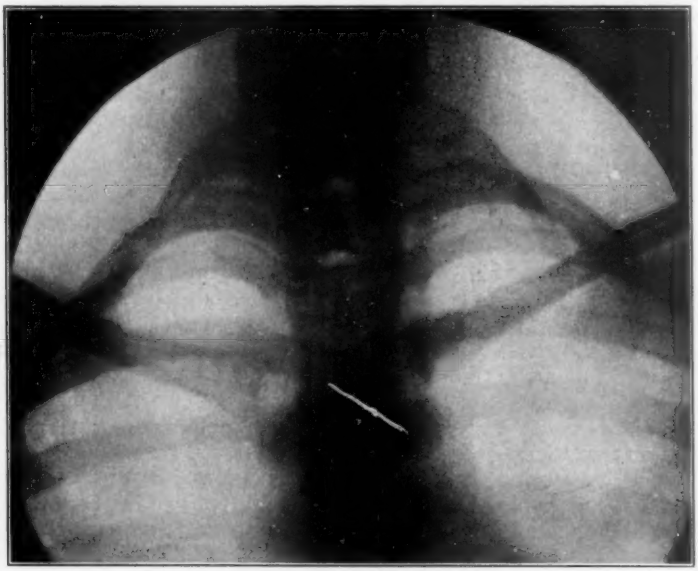

FIG. 1.—Radiogram of Case II. Right side: A well-marked cervical rib, with good head, articulating with the body of the seventh cervical vertebra. The neck, about one-half inch long, ends in a well-formed tubercle. The body broadens, then contracts, extending slightly downward for about an inch, ending in a club-shaped mass, which articulates with the first rib. The slight depression in the rib indicating the position of the artery and the shadow of the vessel itself are more apparent in the plate than in the reproduction. Left side: A rather long cervical rib with an ill-defined head and neck. A large tubercle, which articulates with the transverse process of the seventh cervical vertebra. A slender body about two and one-half inches long ending free.

subclavian artery overlying it at an angle simulating aneurysm. This diagnosis was confirmed by two *x*-ray examinations, one taken shortly after the admission of the patient to the hospital and the other several months later. The *x*-rays further revealed an undetected cervical rib on the left side.

This case is notable because of the position of the subclavian artery in relation to the anomalous rib and the consequent clinical resemblance to aneurysm, for which it had been mistaken. A

similar case is described by Osler,[10] and the question of the existence of true aneurysm in these cases is discussed at length by Keen.[11] Keen believes that in few of these cases true aneurysm will be found at operation or postmortem examination, although several have shown moderate enlargement of the artery, curiously enough distal to the angulation or compression of the vessel, rather than proximal to the obstruction as might be expected. In a case reported by Murphy the artery was flattened. In a case reported by Adams an autopsy disclosed a true cylindrical aneurysm.

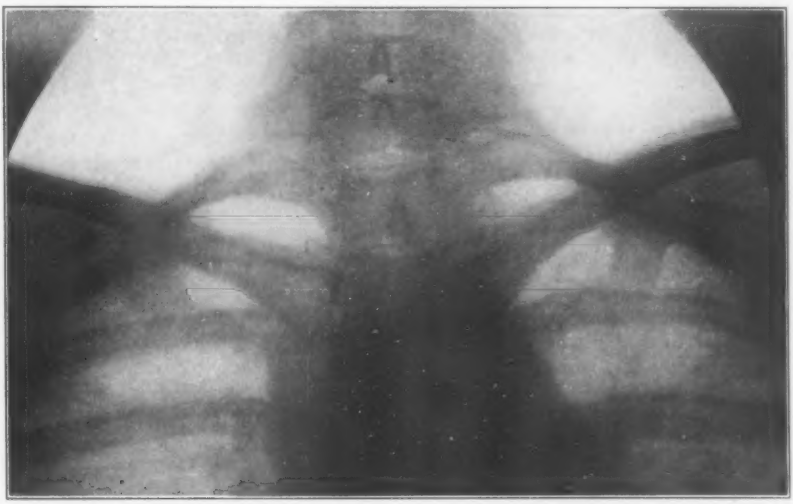

FIG. 2.—Radiogram of Case III. This patient has two well-formed cervical ribs, one on each side. They both have small heads with good necks, tubercles which are well developed, both articulating with the transverse process of the seventh cervical vertebra. The bodies are about one and one-half inches long, tapering toward the middle as they extend downward and outward, and ending in club-shaped masses lying near the first rib.

CASE III.—C. F., female, aged twenty-nine years; unmarried; born in the United States. Applied for examination at St. George's Tuberculosis Class in February, 1911. Family history negative. Past history of measles and pertussis in childhood. She had pleurisy nine years ago, with an attack of "bilious fever" (probably tuberculosis). Two years before this patient had been sent to Stony Wold Sanatorium in the Adirondacks for incipient pulmonary tuberculosis in the right apex. She was under treatment there for one year, and was discharged as an arrested case. Shortly after her return from the mountains she was operated upon for appendicitis. Since

[10] AMER. JOUR. MED. SCI., 1910, cxxxix, 469. [11] Loc. cit.

that time she has been in apparently good health. There have been no symptoms referable to cervical rib. She came to St. George's Class solely for observation of her lung condition. Physical examination revealed a prominent bony mass in the left supraclavicular fossa, which percussed flat and obscured the underlying apical resonance and breath sounds. A diagnosis of left cervical rib was made, which was subsequently confirmed by *x*-rays, the plate revealing also a right cervical rib. Signs of a healed lesion at the right apex were the only other findings on physical examination. The spine was negative.

This case is chiefly interesting for the size and prominence of one cervical rib, with an entire absence of pressure symptoms. In this case there had been a tuberculous process in the apex, but on the side of the unrecognized rib, and possible retraction of the apex following healing, if such occurred, gave rise to no symptoms.

Case IV.—B. S., female, aged thirty-two years; married; housewife. Born in Russia. She was brought to me in March, 1911, by Dr. William Narins. She had been under his observation for some time previously, and was a case suspected of pulmonary tuberculosis with double cervical ribs. The family history was negative. The patient's previous history was suggestive of tuberculosis. She had had several slight attacks of hemoptysis. Physical examination showed prominent supraclavicular fossæ, with dulness on percussion and distant breath sounds. Small masses of bony consistency could be felt at the inner portion of the spaces. No definite signs of tuberculosis could be elicited at this examination. The *x*-rays revealed small double cervical ribs.

It has not been possible to secure this patient for further observation, but she gave no signs of compression and reported no symptoms which could be attributed to the supernumerary ribs.

Case V.—E. L., female, aged forty years; single; stenographer; born in England. Her family history is suggestive. A brother died of "tuberculosis of the spine," and one uncle died of "tuberculosis of the intestines." Her personal history dealt chiefly with several attacks of "rheumatism" in 1903, 1905, and 1907. In the first two of these attacks the joints of the hands and knees were involved. The third attack, five years ago, affecting the right shoulder, was also diagnosticated as rheumatism. In October, 1909, she complained of some disability and pain in the right shoulder and arm, for which she was treated from October, 1909, to March, 1910, without improvement. Later she was told that she was suffering from neuritis, for which she was treated from March to September, 1910, with no better result. Since then she had had no definite treatment for the pain and weakness in the arm, from which she still suffered at intervals, especially after prolonged work. She complained also of some numbness and tingling in the right arm and hand, and found that this hand was easily fatigued.

Physical examination was facilitated in this case by the thinness of the patient, all the bones of the chest being unduly prominent. On inspection the veins of the chest were marked, and there was an evident mass at the inner end of the right supraclavicular fossa with a corresponding depression at its outer extremity. The mass was of bony consistency, immovable, and could be traced backward toward the spine—the familiar characteristics of cervical rib. Further examination of the chest showed extreme prominence of the lower dorsal spines, without other evidence of spondylitis, and of the coccyx. The lungs were negative save for a slight increase in breath and voice sounds at the right apex, not positively beyond physiological limits. The heart was normal.

This case was evidently recognized by some previous observer, as the patient said she was examined several years before with the *x*-rays (fluoroscopic), and was told at that time that she had an "extra rib" which would never give her any trouble. No operative procedure was suggested to her then, or since.

I am enabled to report this case through the courtesy of Dr. Rose Cohen, who saw the patient recently in private practice. The points of special interest are the development of slight but characteristic symptoms at the age of thirty-eight years, and the possible co-existence of healed tuberculous foci in the right pulmonary apex and the lower dorsal vertebræ, suggested by the physical examination taken in connection with the family history.

The *x*-ray examination of this case, made by Dr. Stewart, showed double cervical ribs, the right being the more prominent.

Cases VI and VII were both admitted to my service at Gouverneur Tuberculosis Clinic within the past year. For the reproductions of the *x*-ray plates, I am indebted to Dr. Wise, radiographer at Gouverneur Hospital.

Case VI.—J. S., male, aged twenty-four years; operator; Russian Hebrew. This patient was sent to the Clinic by the United Hebrew Charities Society on the suspicion of pulmonary tuberculosis. His family history was negative, and his personal history was without significance. Five months before admission to the clinic he complained of vague pains in his chest, and later, pains in his legs, weakness, and headache, a familiar group of symptoms in this class of patients. A slight loss of weight during the three weeks he was under observation at the clinic, and the tendency to rapid pulse, were more suggestive. On examination of the chest the patient was seen to have a fairly well-marked right dorsal scoliosis and prominent supraclavicular spaces, in which, upon palpation, the characteristic bony masses suggestive of cervical rib were detected, the left being more prominent than the right. Examination of the lungs showed impairment of both apices, more marked on the right side, with roughened breathing,

but no rales. The heart was negative. Sputum negative. A diagnosis of double cervical rib was confirmed by *x*-ray examination.

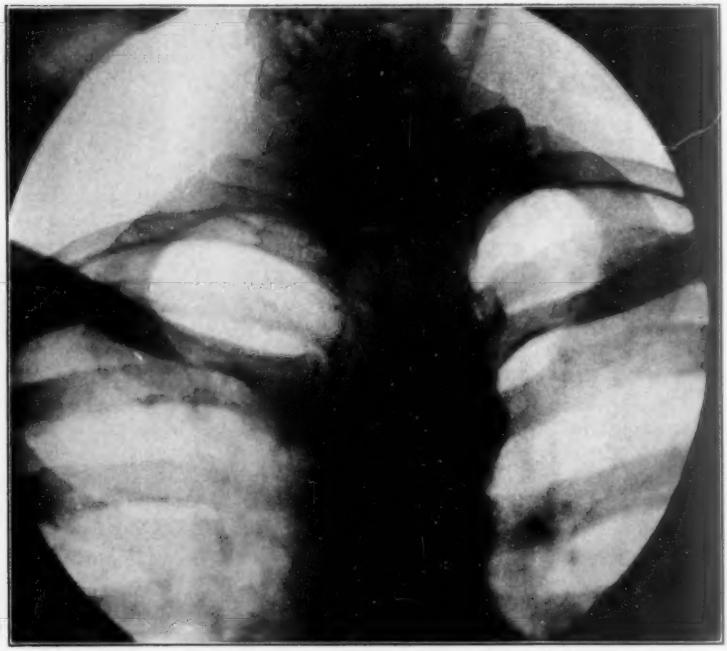

FIG. 3.—Radiogram of Case VI.

This case was the only male in my series. Like all but one of the series, he was examined on the suspicion of pulmonary tuberculosis, and while the physical findings were suggestive only of a healed lesion or inactive process at the apices, the period of observation was too brief for final diagnosis. It is the only case in the series showing well-marked scoliosis. There were no symptoms referable to the supernumerary ribs.

CASE VII.—B. B., female, aged eighteen years; operator on garments; Russian Jewess. She was referred to us by a physician in the district, with the diagnosis of consumption. This diagnosis was confirmed by physical examination. The sputum was also positive. She was an early case, showing only impairment of resonance at the apices with little change in breath sounds and occasional clicking rales after expiratory cough. It was noted, however, that the supraclavicular spaces were prominent, and that the impairment of resonance which corresponded to these areas

was out of proportion to the other pulmonary signs. A diagnosis of double cervical rib was later confirmed by *x*-rays. There were no symptoms referable to the condition, nor have any such developed during the eight months she has been under our observation. She is, however, a progressive pulmonary case, and has recently been sent to a sanatorium. The spine in this case was negative.

In reviewing the cases of cervical rib here submitted, it will be noted that in six of the seven cases pulmonary tuberculosis had been suspected, but that only two of them showed positive signs of the disease (Cases III and VII), and that in only one of these (Case VII) was it an active process. Cases IV and VI were suspicious, but were not under observation long enough for a final diagnosis of the pulmonary condition. Case V may have had a healed tuberculous lesion at the right apex, but it was exceedingly doubtful from the physical signs, and this was the only case with pressure symptoms. Two cases were definitely not tuberculous. One was the cardiac case with physical signs simulating aneurysm (Case II), the other (Case I) was dismissed as entirely negative, and now, after an interval of six years, is still in good health, although recently having slight pressure symptoms on one side. Well-marked scoliosis was observed in only one of the series (Case VI), and that one is the only male of the group.

Only two of the series have presented any symptoms referable to the presence of cervical ribs (Cases I and V), and only the latter of these has suffered any real disability. The symptoms in this instance are apparently due to pressure upon, or stretching, of the lower branches of the brachial plexus, there being no apparent vasomotor disturbance, and in this case only does the question of operative procedure suggest itself. Incidentally this patient is the oldest of the group, and the symptoms in her case did not develop until her thirty-eighth year.

In three instances a diagnosis of unilateral cervical rib was made clinically, but in these, as well as in those cases in which a double rib was detected, the *x*-rays revealed bilateral processes.

In conclusion, the following statements seem to be justified, in summarizing our present knowledge of cervical rib, from the mass of previous evidence as well as from the cases here reported:

1. Cervical rib, especially of the bilateral type, is not of great rarity, probably occurring much more often than it is recognized.

2. It may be recognized clinically in the course of a systematic physical examination, especially in a thorough examination of the chest for pulmonary tuberculosis, and even when there have been no symptoms which might direct the attention of the clinician to the possibility of the condition; but a positive diagnosis of cervical rib cannot be made with certainty without the *x*-rays.

3. The condition is found much more frequently in females than in males, and is often associated with scoliosis; it is not infre-

quently accompanied by pulmonary tuberculosis, although this latter coincidence seems to be without clinical significance except in diagnosis.

4. Cervical rib may occur without symptoms, or with symptoms so slight as not to constitute any inconvenience or disability; and this may be true even when the cervical rib is of unusual size or prominence, as in several of my series.

5. Symptoms may develop at any age, and with or without a history of injury, occupational strain, or other known etiological factor, but they are much more apt to develop later in life and without definite history of causation.

6. In certain cases of cervical rib the abnormal course of the subclavian artery may simulate aneurysm, but true aneurysm is probably infrequent in these cases, and can only be demonstrated by operation or at autopsy.

7. In those cases presenting symptoms of sufficient severity to warrant operation, the resection of the supernumerary rib under recent technique offers every reasonable prospect of complete recovery.

8. In some cases of cervical rib the only clinical significance which can be attached to the condition lies in the fact that the recognition of early pulmonary tuberculosis may be rendered difficult through the presence of the supernumerary rib obscuring definite signs at the apex underlying it; or, of equal importance, that the presence of cervical rib in some cases of suspected tuberculosis may lead to a mistaken diagnosis of apical lesion because of the confusing signs above the clavicle due to the presence of this anomaly.

THE POLYNEURITIC FORM OF ACUTE POLIOMYELITIS: A CLINICAL AND PATHOLOGIC STUDY.

By S. Leopold, M.D.,

INSTRUCTOR IN NEUROLOGY AND NEUROPATHOLOGY, UNIVERSITY OF PENNSYLVANIA.

The question of the existence of a true polyneuritic form of acute poliomyelitis has never been satisfactorily determined. As far as I am aware no case has ever come to necropsy. Wickman in his article on "Acute Poliomyelitis" in Lewandowsky's *Handbook*, published in 1911, states "that he was unable to find in the literature a report of this type in which the peripheral nerves had been studied." Recently, I had the opportunity of studying a fatal case under the care of Dr. Pitfield.

A. S., female, aged twenty years, was admitted to the hospital on August 17, 1911. Nothing of importance was noted in the family or medical history. Her illness began several days previous

to admission with nausea, vomiting, and fever, accompanied by severe pain in the back of the head and neck. A few days later pains and paralysis occurred in both lower limbs, especially the left. Physical examination of the heart and lungs showed no changes. The abdomen was somewhat distended.

The left lower limb was completely and the right lower limb was partially paralyzed, and only the foot could be moved. Pain on pressure over the nerve trunks was noted in both limbs. The left knee-joint was swollen. There was paralysis of the bladder.

No changes were found in the urine. The blood examination showed: Red blood cells, 4,600,000; white blood cells, 7200; hemoglobin, 80. The Wassermann reaction was negative.

August 29. General condition as on admission, save that the patient voids urine voluntarily.

September 18. Pupils equal; reacted to light and accommodation. There were no ocular palsies. The eye-grounds showed no changes. There was no involvement of the cranial nerves. She could move either arm freely, and in all directions. The biceps-jerk was normal. There were no sensory disturbances in the arms or hands. She could move the right foot and leg slightly. The left limb could not be moved at all. Both patellar tendon reflexes were absent. The knee-joints were swollen. Tactile sensation was diminished in both lower limbs. A pin-point was felt over the entire left lower extremity, but not so distinctly over the right lower limb above the knee. There was marked tenderness over the nerve trunks in the lower limbs.

September 24. The urine showed casts and albumin. The condition of the patient remained the same, except that the temperature rose on the thirty-third day, and remained between 102° and 104° until death.

HISTORY. A young adult female, without any previous illness, was suddenly seized with vomiting, fever, pain in the head and back, followed in several days by pain and paralysis in the lower limbs, together with paralysis of the bladder. The important physical symptoms were loss of patellar tendon reflexes and unsymmetric paralysis of both lower limbs, with partial areas of hypesthesia. There was bladder paralysis. In addition there was marked tenderness on pressure over the nerve trunks in the paralyzed extremities, which persisted until death, two months after the onset.

At necropsy the heart, lungs, spleen, and liver showed no changes. The kidneys showed cloudy swelling. A few punctate hemorrhages were seen in the visceral pericardium.

No exudate was noted in the meninges of the brain or spinal cord. The vessels were injected. The cord in the lumbar region was somewhat softer than in the other portions, and on section showed a reddish-gray area in both anterior horns.

Microscopic sections were made from various levels of the spinal cord and medulla oblongata. These sections were stained with thionin hemalum and acid fuchsin, by Weigert's stain, and by the Marchi stain.

Only one peripheral nerve and portion of one muscle were obtained and these were from the anterior aspect of the right thigh, near Poupart's ligament. A portion of the nerve was placed immediately in osmic acid and teased after twenty-four hours. Another portion was placed in Müller's fluid and studied by the Weigert, hemalum, and acid fuchsin stains. There was no evidence of an acute or subacute inflammatory process, and no distinct degenerative changes were noted. The hemalum-acid-fuchsin stain showed slight increase in the connective tissue. There was no round-celled infiltration. The osmic acid showed slight swelling of the fibers, some granulation of the myelin, but no breaking up into droplets. Most of the fibers were normal with Weigert's stain.

The section of muscle showed no round-celled infiltration, no swelling or atrophy of fibers. The striations could be seen, but were not sharply defined.

In the medulla oblongata no changes were noted.

The cervical and thoracic areas of the spinal cord showed no changes.

In the lumbar area stained with the hemalum-acid-fuchsin the meninges showed an intense round-celled infiltration.

The pial vessels were dilated and intensely engorged with blood. Around and within the anterior and posterior roots the round-celled infiltration was intense, and the capillaries were intensely dilated.

The anterior horns showed the characteristic picture of the subacute stage of an acute poliomyelitis.

The left anterior horn was more involved than the right. The capillaries were injected, the round-celled infiltration was marked, and the cells showing a clear protoplasmic area around the nucleus.

Many lymphoid cells, a few connective-tissue and polymorphonuclear cells were also seen. The ganglion cells had practically disappeared as only a few were seen, and those remaining were atrophied. With the Nissl stain the disappearance of the ganglion cells and the varying grades of degeneration of those remaining were most marked.

No changes were seen in the posterior horns or in the white matter. The Weigert stain showed no sclerosis.

These changes were noted in the second, third, fourth, and fifth lumbar segments.

Pathologic History. The changes found in the lumbar region of the spinal cord were those of an acute poliomyelitis in the reparative stage.

The anterior horns were practically destroyed. Intense inflammation was noted in the meninges and around the posterior roots.

Most interesting was the exudate and inflammation of the spinal roots.

The peripheral nerve showed no evidence of a primary neuritis, and the changes present were probably secondary in character.

The diagnosis of this case was difficult. The possibility of a true multiple neuritis had to be excluded. Pain on pressure over the nerve trunks, which is emphasized so much in text-books, could not be considered as a differential symptom.

True multiple neuritis develops slowly, fever is usually absent, special groups of muscles are affected, and the distribution is more symmetric. The absence of sore throat and any history of diphtheria precluded a diphtheritis neuritis, the paralysis in this also occurs much later than the throat disorder; a neuritis of other type, could not with certainty be excluded. The diagnosis of the polyneuritic form of acute poliomyelitis was substantiated by the presence of several other cases in the same vicinity, the unsymmetric involvement of the paralysis, and the absence of cranial nerve involvement, though there are cases of multiple neuritis in which only the spinal nerves are affected, and cases of acute poliomyelitis have been reported with cranial nerve paralysis.

The resemblance of multiple neuritis to poliomyelitis has been known ever since Leyden recognized a clinical relationship.

This similarity in the clinical pictures of the two diseases was recognized in the chronic form of the spinal disease, but recent studies have established the resemblance to acute poliomyelitis.

Cases were described clinically by Strümpell and Barthelmes in 1900. Wickman in 1905 reported a few cases, and in the epidemics observed by Hartman, Foerster, Müller, Mills, and Spiller this form has been recognized. In Foerster's cases everyone showed pain and tenderness on pressure over the nerve trunks, which continued for months. At least clinically there seems to be no question of a polyneuritic form. These cases are remarkable in the prominent part played by the pain over the nerve trunk. After a shorter or longer interval, varying from days to several months, this pain disappears. These cases may recover completely or show permanent paralysis; in rare instances they are fatal.

Those cases in which the pain resolves itself into a hyperesthesia of the skin or on movement of the joints or limbs should not be included in the polyneuritic form. Many cases of acute poliomyelitis may show this at the onset of the disease.

In some of the polyneuritic forms, objective sensory symptoms may be present, such as hypesthesia and disturbances of pain and temperature.

Pathologic evidence of this form is wanting. The peripheral nerves have never been examined in any such case. Cases of acute and subacute poliomyelitis not of the neuritic type have been reported in which the peripheral nerves were studied. In the cases of Redlich, Monkberg, Mott, and others the nerves were

found degenerated. This degeneration could be attributed to a secondary change, owing to the long duration of the cases (from thirteen days to several months).

Harbitz and Schell's cases of acute poliomyelitis, with pain, do not answer to the polyneuritic type, though their findings are of interest.

In their Case VI, a boy, aged six years, had headache, pain in the neck, and pain in the arms. Examination of the brachial plexus and the vagus nerve showed no inflammation or degeneration.

In their Case VIII, one of poliomyelitis, with bulbar symptoms, in which pain played a prominent part at the onset, the vagus, phrenic, and cervical plexus showed no changes.

Their Case X showed an acute onset, with headache, fever, pain in the limbs, and bladder paralysis. No changes were noted in the peripheral nerves.

Wickman believes that the peripheral nerves are never involved and that the pain is due to the meninges, while Raymond held the view that the whole peripheral neuron is affected.

Strümpell, while admitting the involvement of the peripheral neuron, believes that the two diseases are distinct, in that in the spinal type we are dealing with a focal lesion, while in the neuritic form we have the effect of a toxic disturbance in the general circulation.

The pathologic evidence was wanting of any primary degeneration of the peripheral nerve in my case. There were no inflammatory changes. That only one nerve was studied renders this evidence insufficient, but it is reasonable to assume that even this should have shown some neuritis.

Changes may, however, be absent even in true neuritis. Spiller has examined the nerves in different cases of peripheral neuritis, and in some instances he has failed to find any change. This he attributes to the unequal distribution of the inflammatory process, though clinically in his cases the pain was felt along the entire nerve. The more central portions of a nerve may escape when the peripheral portions are diseased. Swelling of the nerve at one portion would produce pain throughout, yet the nerve above the swelling might not show any changes.

Pathologic evidence was not lacking to explain the pain in the case reported. The intense inflammation in the meninges, quite marked around the posterior roots, and the swelling of these roots, on account of the exudation of the round cells within them, as well as the intense engorgement of their vessels, might well account for the pain. The tenderness along the nerve trunks could easily result from this central irritation. In this connection it would be interesting to know whether in other diseases of the spinal cord such as tumor, etc., in which the spinal roots are irritated, tenderness could be elicited along the nerve trunks. That it occurs usually in acute meningitis is well known.

AN INTENSIVE STUDY OF INSECTS AS A POSSIBLE ETIOLOGIC FACTOR IN PELLAGRA.

By Allan H. Jennings

and

W. V. King,

BUREAU OF ENTOMOLOGY, UNITED STATES DEPARTMENT OF AGRICULTURE, WASHINGTON, D. C.

In 1911, Dr. J. W. Babcock, Superintendent of the State Hospital for the Insane at Columbia, South Carolina, brought to the attention of the State authorities, the desirability of an investigation into prevalence and etiology of pellagra.

Following this action, through the initiative of Dr. J. A. Hayne, Secretary of the State Board of Health and Representatives A. F. Lever and Joseph T. Johnson of South Carolina, the writers were, early in 1912, assigned by Dr. L. O. Howard, Chief of the Bureau of Entomology, United States Department of Agriculture, under the direction of Mr. W. D. Hunter, of the Bureau, to investigate the possible relation of insects to pellagra and to gather such data as might serve to indicate whether there was ground for the assumption that blood sucking or other arthropods were involved in the transmission of pellagra in South Carolina.

After several months' work in various parts of the State, we were afforded opportunity to coöperate with the Thompson-McFadden Pellagra Commission of the Department of Tropical Medicine of the New York Post-Graduate School upon its arrival in Spartanburg County. From June 15 until the middle of October, our own studies were carried on in Spartanburg County in collaboration with this Commission, and it is with this portion of our field work that the present preliminary report has to deal.

These studies included the investigation of the premises of pellagrins and of the neighborhoods in which they resided, with special reference to the presence, distribution, and biologies of such insect groups and species as appeared worthy of consideration, after careful study of the conditions.

To this end, we visited the houses of as many as possible of the cases studied by the Commission, and made minute observations of the insect fauna. The patients and their families were questioned in order to obtain such histories as they could give of the attacks or presence of insects and their general experience in regard to the pests with which they were familiar. In many instances the houses were visited more than once, and comparative observations were made under varying conditions. In some instances, the studies were extended to the homes of the non-pellagrous inhabitants of mill villages and elsewhere and the data thus gathered were used to

confirm and extend the information obtained from the patients themselves. Sanitary and other conditions which might have a bearing upon the presence or abundance of insects were noted, and the more remote surroundings were inspected and studied in connection with such forms of insect life, occurring in such situations, as might influence the pellagra focus under investigation. When this focus was of considerable importance, with marked incidence of the disease, the neighborhood, as a whole, was investigated comprehensively and all possible facts bearing upon the situation were noted.

As a rule, the persons interviewed were ready to give such information as they possessed regarding the insect pests with which they came in contact. It was fully realized that popular observations of this nature are liable to be highly inaccurate. Great care was therefore exercised in making the inquiries and in sifting the information obtained. Only such reports were recorded as gave evidence of reliability and clearly referred to the insect which was the subject of the inquiry.

The breeding of certain insects was attempted, but owing to the character of the available facilities and the exactions of the active field work, but meagre results were obtained. This phase of the investigation was therefore unavoidably subordinated to that of the entomological side of the general epidemiological study.

Character and Economic Condition of Spartanburg County. The following description of Spartanburg County and its climate is quoted from the preliminary report of the Thompson-McFadden Pellagra Commission:[1]

"Spartanburg County is situated in the northern or Piedmont section of South Carolina. It is forty miles long in a north-south direction, thirty miles from east to west, and contains 762 square miles. Its surface is hilly and broken by a network of small streams and by four rivers which, with their tributaries, flow across the country in a southeasterly direction, one of these rivers forming the county line of the south. The elevation above sea level at Spartanburg, the county seat, is 875 feet. To the northwest, the slope is upward, the northwest corner of the county being situated at the foot of the Blue Mountain range, while to the south and east the elevation becomes somewhat lower than at Spartanburg, but with no precipitate fall, the whole county thus resting upon a plateau over 700 feet above sea level."

There are no considerable swamps or marshes, and small areas of boggy ground in the neighborhood of streams, while not uncommon, were generally found to be negligible in connection with the breeding of insects of economic importance.

"The annual mean temperature, as recorded at Spartanburg, is

[1] Epidemiological Studies, Part I., Amer. Jour. Med. Sci., July, 1913, pp. 44–45.

60° F. While the winters are mild, killing frosts are apt to occur from November to March inclusive, and the normal mean temperature for the months of December, January, and February is about 42° F.

"The total population of the county is 83,465. Spartanburg, with a population of 17,517, is the only city in the county, the remaining population (65,948) being distributed on farms, in cotton mill villages, and among eleven small towns, only two of which have over 1000 inhabitants. The density of population, as a whole, is 109 per square mile; for the rural population (*i. e.*, outside of Spartanburg City), it is 86.5. While in South Carolina, as a whole, the negroes form 55 per cent. of the total population, in Spartanburg County the whites predominate numerically in the proportion of somewhat over two whites to one negro, there being a white population of 57,055, and 26,410 negroes, the percentage being 68.4 per cent. whites, and 31.6 per cent. negroes."

"The chief industry, and almost the only industry conducted upon a large scale, is that connected with the cotton mills. There are twenty-eight cotton mills in the county, each mill supporting its own village. These mills give employment to approximately 10,000 operatives, representing about 4000 families, and a total mill-village population of about 20,000."

EPIDEMIOLOGY. The epidemiology of pellagra in Spartanburg County presents certain features which have a distinct bearing upon the subject of insect transmission, and may be briefly summarized.

The cases considered in this report are distributed among the population as follows: Mill, 151 cases; rural, 77 cases; and urban, 51 cases.

Divided according to sex, there are: Male cases 71, or 25 per cent., female cases 211, or 75 per cent., or three females to one male.

These are distributed as follows: Mill cases, males, 38; females, 113. Rural, males, 19; females, 58. Urban, males, 11; females, 40.

The racial distribution shows 257 cases among the whites to 25 among the negroes, a ratio of 10 to 1.

The economic condition of the cases may be thus summarized: 85 per cent. were in poor circumstances; 15 per cent. were comfortable; and 2 per cent. were affluent.

The age of the males and females affected is shown as follows: Under five years, 21; five to nine years, 22; ten to nineteen years, 28; twenty to forty-four years, 158; and over forty-four years, 53.

By sex and age, cases appear as follows: Under five years, males, 10; females, 11. Five to nine years, males, 12; females, 12. Ten to nineteen years, males, 7; females, 16. Twenty to forty-four years, males, 16; females, 148. Over forty-four years, males, 25; females, 27.

SEX INCIDENCE. The sex incidence presents striking features. As shown above, the proportion of female to male cases is 3 to 1; and statistics for the entire endemic area in the United States show that this is the approximate ratio throughout.[2] So pronounced an inequality must be based upon some fundamental difference either in environment or physiologic organization of the sexes. It is difficult to account for the inequality upon the ground of great female susceptibility, as such susceptibility is contrary to medical experience and to the well recognized natural law that the female in general is more resistant to adverse influences than the male. Cases of pellagra originating in institutions for the insane have also shown an approximately equal distribution among males and females.[3]

Beall[4] has sought to explain the inequality in sex incidence by associating the immediate cause of pellagra with the dwelling, calling attention to the high rate among females whose time is largely spent about the home, and to the fact that a large proportion of the male cases occurs during the ages when the association with the home is closest, that is, among children and the aged; men during their active years escaping to a great degree.

Of the 282 cases studied, 211, or 75 per cent. were females, of whom 173 were adults; and of these adults, 142, or 82 per cent. were engaged in housework most or all of the time. The adult female population of the mill villages, divided between mill operatives and those who devote themselves mainly or exclusively to household occupations, afforded an opportunity to compare two classes living under seemingly identical conditions with the exception of those of occupation. Of this class, there were 88 female cases, of whom 60 cases, or 68 per cent., gave all or most of their time to housework; the remaining 28 women, or 32 per cent., were engaged in mill work for a portion or all of their time. This disparity, marked as it is, becomes more striking when only those engaged exclusively in house or mill work are compared. Her we find but 12 cases among those who work in the mills, while 46 women, who were occupied exclusively with housework, were affected, the percentages of these groups being 13.6 and 52 respectively. Thus it is seen that a close correlation appears to exist between pellagrous incidence and the amount of time spent in or about the home, and that this holds, not only when the sexes are compared, but within the sexes, themselves.

A marked characteristic of pellagra in all countries is its rural nature. Although the disease sometimes appears to originate in

[2] S. A. Roberts, Pellagra, St. Louis, 1912. K. H. Beall, Bull. Texas State Board Health, 1911, v, No. 9. Tennessee State Board Health, Report on 316 Cases of Pellagra, 1911. C. H. Lavinder, Reprint from P. H. Rep. 65, 1911. R. M. Grimm, P. H. Rep., 1911, xxvi, No. 38.

[3] H. Douglas Singer, Report Pellagra Commission, State of Illinois, 1911.

[4] K. H. Beall, Loc. cit.

cities of considerable size, an analysis of conditions in such cities will usually, if not always, show that in certain important aspects, the rural element governing the presence and abundance of insects is predominant.

Isolated sporadic cases of a disease are highly suggestive of an insect carrier, under certain circumstances, especially when exposure of the individual to infection by association with other cases may be excluded. The suggestiveness is strengthened, in the case of pellagra, by the existing evidence against direct contagion and also by the low degree of infectiousness which the disease appears to exhibit.

Another fact which may point to the agency of an insect in pellagra transmission, is the occurrence of several cases in a single family, and this frequently happens. It is obvious that the close association of persons constituting the household would increase the opportunity for transmission by predatory insects. This feature is emphasized by what appears to be a definite chronological connection between such cases.

At the same time, the large number of instances in which but a single member of a household is affected, does not preclude the same possibility. It is conceivable that by reason of habits or constitution, the unaffected members, might, for a time, altogether escape infection. Or, scarcity of the insect carriers, especially if conditions favor their free entrance into and departure from the house, may lessen the chances of transmission within the home.

Attention may be directed to some features of the epidemiology of pellagra which suggest a certain analogy to those of two other diseases, viz., malaria, an insect-borne protozoal disease often of chronic character; and acute anterior poliomyelitis, which, as apparently shown by certain recent experiments, may be transmitted by biting flies, thus strongly indicating at least one of the channels for the communication of that disease.

The seasonal recurrence of pellagra and its period of greatest development during the summer months, the period of greatest insect activity, finds an approximately similar condition in malaria and probably a greater similarity in the case of poliomyelitis. Both of these diseases are largely of rural origin, as is pellagra. Poliomyelitis, moreover, is marked by the occurrence of sporadic cases, not to be explained by contact infection and there is a lack of evidence of direct contagion, two facts which are true of pellagra.

The Insects Studied. While the object of our investigation was the study of all insects which may have any part in the transmission of pellagra, it was realized that a careful consideration of conditions and of the insect fauna would inevitably narrow the field to a few genera and species. It became clear that efforts might safely be concentrated upon a few groups of insects, mostly of blood-sucking habits. Keeping in view the conditions which

are imposed by the facts of disease transmission by insects, the following groups were given careful attention: Diptera, or two-winged flies; Hemiptera, including the lice and bed-bugs; Siphonaptera, or fleas, and Acarina, or ticks. Some attention was also paid to the roaches, Blattidæ.

ACARINA. The ticks of the family Ixodidæ must be mentioned, although their importance in this connection is negatived by their habits, life history and the infrequency with which the persons who suffer most from pellagra appear to come in contact with these arthropods in Spartanburg County.

It will be remembered that most ticks of the family Ixodidæ (no members of the family Argasidæ occur in Spartanburg County) require three hosts during their period of development, dropping to the ground on the completion of each stage and reattaching themselves to another host, sometimes of a totally different species, when they have advanced to the next stage of their existence. The chances of any tick of this group attaching to successive *human* hosts are remote. It is unusual for these parasites to remain undiscovered on man long enough to complete the stage during which attachment was effected. Almost certainly they are removed and killed and transmission of infection from the first host thereby prevented. The presence of animal reservoirs of infection would therefore seem to offer the only means by which this disease could be transmitted by the group of ticks mentioned and there is no indication that such reservoirs exist. Reports from pellagrins and non-pellagrins of attacks by ticks were rare and in the course of the work only two lots of ticks were collected, one lot from dog and one on the clothing of man. Many dogs and other animals were examined and the indication is that the tick infestation of the country is light. *Amblyomma americanum* and *Dermacentor variabilis* probably occur in the county. The usual hosts of these species are dogs but they are known to attach to man.

It is impossible to explain the sex incidence of pellagra by the incrimination of ticks, men being obviously more exposed to their attack than women. In view of this fact and the lack of evidence that animals are subject to and can serve as reservoirs of pellagrous infection, the almost certain death of all ixodid ticks which bite human beings, together with the equal certainty that not all pellagra sufferers in the region can have been exposed to the bites of ticks, these arthropods can safely be excluded from among the possible factors of pellagra transmission.

PEDICULUS VESTIMENTI AND CAPITIS. Head lice (*Pediculus capitis*) were locally said to be far from rare among certain classes of the population, but this statement is not borne out by our observations or by reports received. Only one or two reports of previous experience with the parasite could be obtained, and the writers saw but one case of actual infestation. As reports regarding such insects

as bed-bugs and fleas were usually frankly given, it seems hardly probable that reticence could account for the many negative reports in regard to *Pediculus*. We are forced to believe that whatever may be its prevalence, it is far from universal and entirely inadequate as a possible agent in the transmission of the disease. That a wingless insect with the habits and associations of the head louse can be the cause of infection in any but a very limited class of cases, is scarcely to be credited, and such an inference leaves the question of female preponderance and sporadic cases unsatisfactorily answered.

It is well known that head lice will, upon occasion, be transferred from infested to clean persons, but observations indicate that unless the infestation is gross or the association of persons is intimate such transfer of the parasite is not particularly common, and this is borne out by the experience of persons of ordinarily careful habits. We are unable to see that the head louse can be incriminated when we consider its rare occurrence upon persons of fastidious habits, who yet furnish an appreciable number of cases of pellagra.

No reports of *Pediculus vestimenti* were received and no observations of the species were made. The evident rarity of the species as well as its habits exclude it from consideration as definitely as the foregoing.

CIMEX LECTULARIUS. The bed-bug (*Cimex lectularius*) was found to be of practically universal occurrence in the houses of the largest class of pellagrins of the region. Of 256 reports received from pellagrins, the actual presence or recent attacks of bed-bugs were admitted in 241 instances. Only 15 persons denied that they had been exposed to this pest, and from their known prevalence in the mill villages and elsewhere some doubt may be entertained as to the accuracy of at least some of the negative reports.

Concerning the incrimination of *Cimex* in pellagra transmission, there is one fact which alone is sufficient to indicate its innocence. This is the sex incidence of the disease. It has never been shown that *Cimex* attacks females more frequently than males, certainly not in the proportion of 3 to 1, or if adults in the prime of life are considered, of 9 to 1. If this is not the case, the explanation of transmission by the insect is unsatisfactory. In the often crowded, badly infested, and none too cleanly homes of a considerable class of pellagra sufferers, indiscriminate attacks of the insect are greatly facilitated and must certainly be made upon the inmates without regard to age or sex.

It is well known that the bed-bug has the power to endure starvation for extended periods, and nothing is more difficult than eradiction of the pest when it has once taken possession of a building. If it were capable of conveying pellagrous infection, these qualities might account for what has been termed the "place infection" of pellagra. At this time, proof is lacking of such a source

of infection, but should it be shown to exist, the facts of sex incidence just cited together with the occurrence of but one case in a family in many instances must stand opposed to incrimination of the insect.

While but 2 per cent. of the pellagra cases studied were in affluent circumstances, others of this class have come to our notice in other localities, and it may be asserted that such cases are by no means rare. It cannot be questioned that the habits of life and general associations of such persons greatly minimize the possibility of their infection having been brought about through the agency of the bed-bug.

Specimens of this species were collected in connection with some cases, but no special effort was made to do so in the majority of instances. No systematic search for a causative organism was being prosecuted nor transmission experiments carried on in the field. It was therefore considered that the value of actual collections of bed-bugs, systematically made, hardly justified the time required and the interruption caused to the routine pursued in securing case histories of pellagrins. In addition, the positive reports generally received, supported by occasional collections seemed amply sufficient to establish the almost universal presence of the pest.

BLATTIDÆ. Of roaches, only the common cockroach, *Periplaneta orientalis* and the smaller *Ectobia germanica* were encountered. These disagreeable household pests were found to be abundant and generally distributed, but nothing remarkable was noted in their relations to the homes of pellagra cases or of the population in general.

Though armed with strong, biting jaws which enable the insects to commit serious injury to leather and other substances there are few accounts in the literature of attacks upon human beings, and these seem to be confined to nibbling of toenails, eyelashes, etc. Even such as they are, attacks upon man must be considered exceedingly rare, and they cannot be considered a factor in transmission.

The well known habit of roaches of frequenting kitchens and larders, their omnivorous habits, and the inefficient protection of food too frequently practised by the classes who suffer most from pellagra suggest the possibility of its transmission by food contamination. If such means is possible the part played by the insects must be far less important than that of house flies, for the exposure of food to the latter is unquestionably greater and the carriage of fecal matter far more regular and constant than can be the case with roaches. Certain experiments conducted by one of us (A. H. J.) indicate that roaches will not readily feed upon such material and under normal conditions their opportunities for the

contamination of foodstuffs with human excreta are far less than those afforded house flies.

Roaches can, therefore, not be considered an important element in pellagra causation and must be considered in the same category with, but far inferior to, the house fly.

TABANIDÆ. Flies of the family Tabanidæ, which includes the well-known horse-flies, were rare in Spartanburg County during the season of 1912. One or two specimens of *Tabanus atratus* (?) were seen flying about our automobile while in motion, but none were captured. Only two specimens of Tabanidæ were collected in Spartanburg County and these were unfortunately lost before exact determinations were made. The flies of this group are primarily a pest of the larger domestic and also of wild animals in localities where the latter are found, and their habits are such as to exclude them from the possibility of an active role in pellagra transmission. In localities where Tabanidæ are numerous the biting of human beings is by no means uncommon, yet even in such regions bites are scarcely received with the frequency and regularity which are essential to the transmission of human disease in the absence of an animal reservoir of infection.

The comparative scarcity of these flies in Spartanburg County where pellagra is prevalent is the reverse of the conditions of the country near the Atlantic coast where tabanids are exceedingly numerous and pellagra comparatively rare.

SIPHONAPTERA. In our studies, fleas were given particular attention on account of their known role as carriers of certain diseases and the fact that in certain localities they are very abundant and annoying pests.

It must be understood that, except where otherwise stated observations and conclusions regarding fleas refer strictly to conditions in Spartanburg County.

Somewhat to our surprise we found that, in the region studied, fleas, so far as attack on human beings is concerned, seemed to be almost of negligible importance. Reports were obtained from 154 pellagra patients or their families and of these but 10 gave positive accounts of attacks by these insects. Assuming that the reports were reliable, this may seem a remarkable condition, and allowing for a certain percentage of inaccuracy it is still practically certain that these insects are not a universal or constant pest of human beings in the locality.

While persistent attacks of fleas upon man are comparatively infrequent in Spartanburg County, they are much more common in the low sandy country lying between the Piedmont region and the coast. In the latter section the prevalence of pellagra is slight when compared with the region of which Spartanburg County is a part.

The human flea, *Pulex irritans*, is uncommon even if it exists

in Spartanburg County. We failed to find this species upon any of the numerous animals examined, nor did we succeed in collecting it from human beings.

Ctenocephalus canis and *Ctenocephalus felis* were taken on numerous dogs and cats. *Echidnophaga gallinacea*, the chicken flea, is a not uncommon pest of fowls, occurs with some frequency upon cats, dogs, and domestic rabbits, and in one instance, a report of its attack upon human beings was obtained.

In view of the fact that cats and dogs are very commonly kept, and that these animals were found to be practically always heavily infested with their respective fleas, it might be assumed that attacks upon human beings would be of common occurrence. Several reasons for doubting this assumption may be advanced. While the cat and dog fleas are less fastidious in their choice of host and more tolerant of abnormal host species than many other fleas, it is nevertheless quite certain that these species are less frequently a human pest tnan is usually supposed. Attacks by them upon man are not uncommon, but under ordinary conditions, even in the presence of infested animals, it by no means follows that persons associating with the animals will be infested.

It has been personally noted by one of us, in another locality, that in a house in which cats heavily infested by *Ctenocephalus felis* were kept, the fleas which were a frequent source of annoyance to the human inhabitants were all found to be *Pulex irritans*. Eggs from the flea-infested, long-haired cats must have been freely dropped about the floors, which offered excellent conditions for the development of the insects. It is equally certain that adult fleas were lost from their feline hosts, yet during a period of more than a year, every flea which annoyed the members of the household was carefully sought for and collected. They were all *Pulex irritans* and it is noteworthy that their attacks were usually made at night.

This extreme instance is cited to indicate that except at times of unusual abundance the fleas of domestic animals are not likely to attack human beings freely. It is true that individual fleas of cats and dogs ordinarily remain on human hosts but a short time, frequently leave him without biting and are probably but rarely transferred directly from man to man, factors which would tend to lessen the probability of their acting as carriers of a purely human disease.

The number of domestic animals kept by pellagrins or their families is of interest in this connection. Of 227 instances in which notes were made regarding the keeping of the smaller flea-bearing domestic animals, cats or dogs were kept in 120 cases, or 53 per cent., while none were kept in 107, or 47 per cent., of cases. This is significant in connection with the host habits of fleas which have just been discussed. If human beings in Spartanburg County

are freely and regularly attacked by fleas derived from cats or dogs, which are usually heavily infested, it seems remarkable that in so few instances were the keepers of these animals able to report their noticeable presence.

Of the 10 cases reporting attacks of fleas, dogs or cats were kept in 9 instances and none were kept by but one family. This is too small a number upon which to base conclusions. There were 149 cases in which data were secured on both the keeping of cats or dogs and the attacks of fleas. Animals were present in the houses of 78 of these cases and absent in 71. Of the former, 9 reported attacks of fleas, while, of those who kept no animals, but 1 gave such a history. The ratio of the number of reported attacks, by families in which cats or dogs were kept, to those by families with none of these animals is therefore 9 to 1 and seems to indicate that when fleas are troublesome, domestic animals are the usual source. In connection with the figures relative to the number of animals kept, it is also indicated that these animals by no means always cause the infestation of their human associates.

Sixty families who kept domestic animals and 70 who kept none, reported no attacks of fleas.

The presence of rats was reported in 38 cases, and of mice in 124. In spite of efforts to secure specimens of rat fleas, it was possible to do so in only one instance so that the degree of infestation of the rats of the region and the species occurring upon them could not be learned. The single rat secured has been determined as a cross between *Mus rattus* and *Mus alexandrinus*. The fleas with which this rat was infested proved to be *Xenopsylla cheopis*, the Indian rat flea. The occurrence of this flea at a point so far inland is interesting as is the species of its host, an animal with which it is intimately associated in the East and in many parts of its littoral range.

The facts opposed to the incrimination of fleas in pellagra transmission are: those of the sex incidence of the disease, its association with the home, the host habits of fleas, the comparative infrequency of their attacks upon human beings in the districts suffering most heavily from the disease and the inverse ratio of their abundance to the occurrence of pellagra.

In consideration of these facts it is impossible to base any satisfactory theory of transmission upon the agency of these insects.

CULICIDÆ. The abundance of mosquitoes, both of species and individuals, their agency in the transmission of important human diseases, their persistence in seeking blood and in certain instances, their close association with man cause these troublesome pests to assume a position of the highest economic importance.

Although present to a greater or less degree in most parts of Spartanburg County, they are few in number in comparison with those present in many less favored localities. The topographical

features of the district have much to do with this condition, and owing to the conformation of the land and the character of its drainage, extensive breeding areas do not exist.

When this group is considered in connection with the possibility of pellagra transmission, certain salient facts are to be noted.

The longevity with which some mosquitoes are known to be endowed, their great abundance and the predilection displayed by certain species for man's vicintiy, appear to fully qualify these insects for the role of transmitters of human disease. This is amply shown to be true by the number of diseases which are transmitted by them.

Furthermore, mosquitoes are readily transported in various ways other than by their own flight to places far distant from their original habitat, with the attendent possibility of spreading infection.

Their power of flight renders the carriage of infection from house to house an easy matter, although the distance travelled is probably not great in the case of house mosquitoes and ordinarily the radius of infection conveyed by them would be correspondingly short.

It is unquestionably an argument, though not necessarily a conclusive one, against the incrimination of mosquitoes in pellagra transmission that no one species, occurring in endemic regions, has a range as wide as the geographical distribution of the disease and different species would necessarily (if the group be incriminated) assume the role of transmitters in different parts of the endemic area.

It is possible, were pellagra transmissible by mosquitoes, that several species might have the power to transmit the disease, yet there is often a high degree of specialization in insect vectors. In view of the nice physiologic adjustment between the insect host and its parasite, which is evidently necessary to the function of transmission, the foregoing assumption is not necessarily valid.

The most important fact which is opposed to the agency of these insects is the preponderance of cases among females and especially among home-keeping females. If, as indicated, the disparity is due to the greater exposure of women to infection, a cause must be sought which affects this class only and excludes those classes which show a low pellagrous incidence. In other words, the cause must be active in the day time when housewives, children, and old men are largely at home and which does not operate at night when all ages and sexes of the household are within the home influence. It is illogical to seek the cause in an insect whose activities are confined to the night hours, however well it may otherwise conform to the epidemiological and other facts of the disease.

It is to be noted, as we have said, that while mosquitoes are, comparatively speaking, not abundant in the Piedmont region

where pellagra abounds, they are a more serious pest and infinitely more numerous in the low-lying country near the coast where pellagra, though not absent, is by no means abundant.

While a very considerable number of our cases reported attacks of mosquitoes, more than an appreciable percentage of these referred to localities beyond the bounds of our terrritoy, largely to places in the low country below the Piedmont.

The scarcity of mosquitoes was noted by all members of the party and it is highly probable that their number falls short of that required for effective disease transmission. It is admitted that diseases fail of transmission and cease to exist even in the presence of their known carriers when the number of the carriers falls below a definite point.

Certainly, it will hardly be asserted that a group of insects, represented so sparingly as are mosquitoes in this locality, can be the agent of causation of a disease having the activity displayed by pellagra in this region at the present time.

Culex quinquefasciatus and *Culex restuans* are the principal species recorded by us. *C. quinquefasciatus* was taken at a number of points and is, as might be expected, widely distributed in the county. Some water barrels were heavily infested and were producing enough mosquitoes to infest the entire immediate neighborhood. *C. restuans* is rather widely distributed and probably ranks with *C. quinquefasciatus*, as a general nuisance. *Aedes calopus*, the yeallow fever mosquito was not taken within the county although quite ample facilities for its propagation exist. It is undoubtedly introduced, probably every year, but appears not to be a constant resident, the winters being usually too severe to admit of its survival. It can have no importance in the present connection in spite of its day biting proclivities and house haunting habits. Its geographical range is not as wide as the distribution of pellagra and it thrives as well in large cities as in small.

Spartanburg County bears the reputation of being almost entirely free from malaria, a reputation sustained by the small number and especially the character of the anopheline mosquitoes recorded by us. *Anopheles crucians*, a host of the estivo-autumnal parasite was encountered but once. The only other species observed was *Anopheles punctipennis* whose incrimination in malaria transmission remains somewhat doubtful. This species was met with chiefly in the vicinity of Spartanburg, a place whose physicians unanimously declare to be free from endemic malaria. Of 240 pellagra patients questioned as to the biting of mosquitoes, 160 gave positive reports while 40 only were negative.

SIMULIDÆ. Although but recently incriminated in disease transmission, the flies of the genus *Simulium* have long been known in both Europe and America as a serious pest of man and animals, their visitations assuming in certain regions the proportions of a

scourge. Much has been written regarding their blood-thirstiness and the intolerable nature of their onslaughts, the heavy loss occasioned among all kinds of domestic animals and even the death of human beings. Some of the accounts of their depredations seem to bear the stamp of a vivid imagination, but the more conservative and scientific statements, especially those of later years, are sufficient warrant for classing them among the more important and blood-thirsty of predaceous insects.

The attractive theory propounded and defended by Sambon, that these gnats are the active agents in the causation of pellagra has brought them into prominence from a new point of view.

He bases his belief in the agency of the Simuliidæ upon the following: *Simulium* affects the same topographical conditions as pellagra; in its adult state, it seems to present the same seasonal incidence; it is found only in rural districts and, as a rule, does not enter towns, villages, and houses; these flies cause severe epizoötics in Europe and America. The disease, he finds, is limited to agricultural laborers (to be explained satisfactorily only by the incrimination of the gnats); the range of the group seems to cover that of pellagra, although indeed it exceeds it.[5]

Knab has pointed out that close association with man is one of the essential factors in disease transmission by insects, when, as premised by Sambon in the case of pellagra, the disease is of parasitic origin and the organism is present in the blood stream.

Simulium inhabits regions in which pellagra is endemic and in many well-watered localities presents a picture of distribution which completely covers every part of large areas. Its numbers are often great enough to cause annoyance and even injury to all warm blooded inhabitants, yet in spite of these phenomena it can not be said to show the association with man to which we have referred. The species of *Simulium* are essentially "wild" and there is no evidence, in what is known of their life history and habits, that repeated attacks on human beings with intervening periods of, at least, several days can take place with sufficient frequency to confer upon the insect the character of an effective disease tranmitter. As Knab cogently insists: "It is not sufficient that occasional specimens bite man, as for example, is the case with forest mosquitoes. Although a person may be bitten by a large number of such mosquitoes, the chances that any of these mosquitoes will survive to develop the parasites in question (assuming such development to be possible) and then find opportunity to bite and infect another person are altogether too remote."[6]

Although Knab cites, as an example, the forest mosquitoes, the

[5] L. W. Sambon, Progress Report Investigation Pellagra, Jour. Trop. Med. and Hyg., October 1, 1910, xiii, No. 19.

[6] Frederick Knab, Unconsidered Factors in Disease Transmission by Blood-Sucking Insects, Jour. Econ. Ent., 1912, v, No. 2.

principle is of wide application and includes within its scope the species of *Simulium*, which, indeed, he excludes upon this very ground, from consideration as potential transmitters of disease.

It must be borne in mind that the essential factor here, is not the possibility that an occasional individual might sometimes be able to fulfil these conditions, but rather that the group lacks the habits (of close association with man) necessary to the establishment of the biologic relations between the vertebrate host, the invertebrate host, and the parasite of the disease.

Our observations of the group in Spartanburg County are strongly corroborative of the foregoing. We found *Simulium* breeding near or even within the limits of mill villages as well as of towns, but we failed to detect the slightest disposition on their part to seek out and attack man, to come about his dwellings, or to come in contact with him in any but the most casual and incidental manner.

FIG. 1.—Stream at edge of mill village. A breeding place of *Simulium tenuatum*.

The assertion that these flies cause severe epizoötics is certainly not supported as regards America, at least. The heavy loss of domestic animals which occurs during severe visitations of the gnats can not be attributed to any specific disease which is com-

municated by them. All the evidence indicates that death is caused by the venom injected and by the worry and irritation occasioned by the myriad bites.[7]

Individuals are carried to or through mill villages as well as other communities, upon animals (in the ears of horses and to a less extent on cattle). This might be a limited source of supply for localities removed from the vicinity of the breeding grounds of the fly. However, it is not even known that, after a full engorgement, the female will seek a second blood meal. The extreme degree with which the flies distend themselves with blood, when undisturbed during biting, coupled with the probably short life of the adult insect, suggest that they do not ordinarily bite again.[8]

Species of *Simulium* are unquestionably found in numbers in large areas of country in which pellagra is rampant, but there is evidence to show that, contrary to Sambon's assumption, the disease is found where *Simulium* is not. We have information that pellagra occurs endemically in Barbados and as yet not only has no species of *Simulium* been found in the island, but its physical characteristics entirely preclude the existence there of the fly.[9] There are arid regions in the United States in which the same situation exists but under different conditions and there are still other localities where these gnats are far too rare to satisfactorily account for the cases of pellagra originating in them.

That the extension of the range of *Simulium* beyond the limits of pellagrous endemicity is certainly, as Sambon says, no argument against its incrimination for there are many localities inhabited by insects with known powers of disease transmission, yet which are entirely free from the diseases which these insects may confer. In the absence of the human carrier of infection and the proper conditions, the insect vectors are innocuous.

The seasonal appearance of *Simulium*, which is supposed to correspond with that of pellagra, is probably of less significance than has been assumed. The studies of the Commission have shown that the spring-fall recrudescences of the disease do not occur, with the intensity ascribed, at least in the area under consideration,[10] although the period of greatest abundance and activity of *Simulium* appears to be here, as in Italy, the early spring. Until more light is thrown upon the length of the incubation period of the disease, which seems to be variable, assumptions as to the exact time at which infection is incurred, must be received with reserve.

The disease is of essentially rural distribution but in South Carolina, it occurs in towns of considerable size. As has been

[7] C. V. Riley, The Southern Buffalo Gnat, Report of Comm. Agric., United States Dept. Agric., 1886.

[8] C. V. Riley, ibid.

[9] Personal letter from Dr. H. A. Ballou, Imperial Entomologist, Barbadoes.

[10] J. F. Siler and P. E. Garrison, An Intensive Study of the Epidemiology of Pellagra, loc. cit.

pointed out, in these places the rural element, as regards insect life, is predominant and the conditions do not necessarily preclude the occurrence of rural diseases.

In the classes of the population affected by pellagra, a very marked contrast appears to exist between European and American conditions, if European reports are accurate. The practical confinement of the disease in Italy to agricultural laborers, a class living under conditions of abject poverty, finds no economic or occupational parallel in America. Although, in Spartanburg County, the farming class furnishes a considerable percentage of all cases, the highest incidence of the disease is found among inhabitants of mill villages, whose conditions and habits of life are radically different in most essential features from those of the Italian peasant.

The fact that more than one species of *Simulium* would have to be involved to cover the entire range of pellagra is not a convincing argument against incrimination of the group but it lessens, to a certain degree, the probability of their agency. (See page 422 on mosquitoes.)

It seems to have been assumed that because the many streams of a well-watered country are infested with the larvæ of *Simulium*, the inhabitants of that country, especially those living in close proximity to streams, must be exposed to and incur the bites of the gnats.

Knowledge of the biting habits of the American species is incomplete, but it is clear that some of these species show great irregularity in their practice of seeking blood. The variation in the exercise of this habit seems to have in it a large geographic, or possibly, topographic element, for a species may be a serious pest of man in one part of its range, yet seem to ignore him entirely in another. Thus, *Simulium venustum*, one of the so-called "black flies" while proverbial for its onslaughts in the Maine woods, is only moderately troublesome in the Adirondack Mountains. In the mountains of Henderson County, North Carolina, these flies were found by one of us to be exceedingly abundant but offering no attack to man though this was courted. Sitting or standing quietly with small swarms of the flies "dancing" about the head, no attempt was made to bite. This occurred both in the presence and absence of animals which in the former case were being actively attacked. Persons of intelligence who were questioned, denied that the flies bite people and in only one instance was such a report elicited. In this case the identity of the fly was open to question, although probably a *Simulium*.

Similarly, *Simulium vittatum* is known to bite man in some parts of its habitat, but on excellent authority it is stated that in Idaho it "does not bite people."[11]

[11] Personal Letter from Prof. J. M. Aldrich.

Such variation in biting habits is not without parallel among blood-sucking flies, as *Glossina palpalis* is reported by Steudel to bite man on Victoria Lake but not on Lake Tanganyika.[12]

This variability is of special significance, for it points to the fallibility of deductions based upon the mere presence of *Simulium* larvæ in a given locality without regard to the species represented and the *local* biting habits of that species.

Simulium pictipes, a widely distributed and often abundant species, does not bite man at all.

So numerous are the streams in the county that the homes of 275 pellagrins stood within an average distance of 210 yards from running water, and 215 of these streams were found to be infested with *Simulium*.

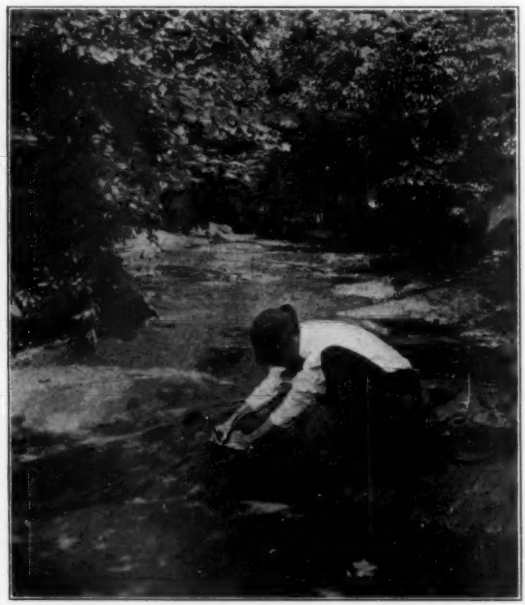

FIG. 2.—A typical breeding place of *Simulium pictipes*.

In spite of this fact, but 16 cases reported attacks of flies, the description of which could with any probability of truth, be interpreted as referring to *Simulium*. Great patience was exercised in eliciting these reports and they were carefully weighed before recording.

[12] Steudel, Deutch. Kolonialblatt, 1912, 15 Mai, xxiii, No. 10, and Beihefte zum Archiv f. Schiffs und Tropenhygiene, 1912, Mai, Beiheft 4.

The distance of *Simulium*-infested streams from the homes of 11 cases reporting bites of the fly averaged 236 yards, no data as to infestation of streams being available in 5 cases reporting bites.

The distance of *Simulium*-infested streams from the homes of 125 cases reporting *no* bites of the fly averaged 221 yards.

This difference in average distance is not actually great but it is interesting nevertheless. It is a striking fact that so large a number of persons living a shorter average distance, many within a few yards, from infested streams should not have been bitten and points forcibly, not only to the uncertain biting habits of *Simulium*, but to the lack of significance in the proximity of streams, even when *Simulium*-infested.

We may add that adult *Simulium* were collected in the immediate neighborhood of 46 cases who reported no bites.

The tenor of these reports is amply corroborated by those of many persons, including a considerable number who were especially well qualified through intelligence and experience with the flies in other localities or who had observed their attacks upon animals in this.

It cannot be questioned that as a pest of man in Spartanburg County, the species of *Simulium* are of small importance and that at most their attacks are delivered locally and are few in number. When comparison is made between this condition and that existing in places (including Spartanburg County) infested by stable flies, sand flies, mosquitoes, etc., the contrast is striking. These insects are always well known, even when not abundant, as we have shown in regard to mosquitoes in this locality. It is practically impossible that *Simulium* could be present and bite man in sufficient numbers and with enough persistence to satisfactorily explain the occurrence and spread of pellagra without being a well recognized and familiar pest.

Three species of the genus were encountered by us within the limits of our territory, namely: *Simulium venustum*, *S. vittatum*, and *S. pictipes*.

The former is by far the most numerous and generally distributed of the three. It was taken in its four stages, adults being collected about twelve times, either in the act of attacking animals or of ovipositing.

Simulium vittatum was taken in the larval, pupal, and adult stages, and also probably in the egg. Adults were twice collected while attacking horses or mules.

Simulium pictipes occurs quite locally in large colonies where suitable conditions exist. These consist of a rapid flow of clear water over boulders and sheets of rock in the larger streams. Such conditions are not very frequently met with in this vicinity owing to the turbidity of most of the creeks and rivers of the locality.

There are no records of this species attacking man and it need not be considered in the present connection.

The facts as set forth above do not support the incrimination of *Simulium* in the transmission of pellagra.

HOUSE AND BLOW FLIES. So abundant is the current literature regarding the nature, habits, and pernicious activity of the house fly, that a general discussion of this well known and troublesome species seems superfluous. Its familiar role as an active mechanical carrier of bacterial disease, however, renders it of the highest economic importance and necessitates its consideration in the present study. The possibility of the transmission of pellagra by house flies through the contamination of food to which they have access, or by direct mechanical transmission of the virus (if it exists) from man to man, is evident.

Musca domestica was present everywhere and was usually extremely numerous. Sanitary conditions were only too frequently such as to attract, if not actually to breed, the filth-loving species of flies, but in the more or less congested village and town communities there was no strict correlation between the sanitary condition of the individual premises and the number of flies present. Even well-kept homes offered sufficient attraction to insure their infestation by the flies which in every neighborhood were present in large numbers.

In mill villages the principal source of house flies appeared to be the accumulations of manure of horses and cattle at the stables and sheds in which the draught animals of the mill companies and the cows of the operatives were sheltered. In those villages in which milch cows are allowed to be pastured and stabled indiscriminately through the village, breeding occurred almost everywhere in the haunts of the animals.

The type and condition of privies in mill villages are conducive to the presence and breeding of this species as well as to the carrion flies, *Calliphora*, *Lucilia*, and the *Sarcophagidæ*. Upon otherwise cleanly premises, the privy was often a source from which flies emanated and was a standing menace of infection.

Musca domestica was found in and about the homes of practically all of the cases studied as well as those of non-pellagrins. In a very few instances case histories make no mention of the species, but this is unquestionably due to inadvertence.

Until the transmissibility of pellagra is disproved or the nature of its virus and the manner of its communication are known, the house fly must be regarded with suspicion.

STOMOXYS CALCITRANS LINN. The biting stable fly is an insect of cosmopolitan distribution and great economic importance. In most localities within its habitat it is very abundant, and though it feeds by preference upon domestic animals, man is very frequently attacked. Attacks upon human beings are more common when the

animals upon which it normally feeds are not available and its onslaughts are often severe and persistent.

The injury inflicted upon live stock is often very serious and many deaths are caused during the occasional outbreaks of this fly, which sometimes occur under unusual conditions favoring its inordinate propagation. At all times it is a serious pest of animals and has been incriminated in the transmission of trypanosomal diseases of animals, anthrax in animals and man, and of anterior poliomyelitis in man.

While *Stomoxys* is, as a rule, more abundant in country districts, owing to the greater facilities for propagation which it finds in the rural environment, it is usually common in towns and cities of even the largest size. In the very heart of the great cities and in such neighborhoods as practically preclude the possibility of its breeding, it may be seen in considerable numbers along the main thoroughfares. The vicinity of markets and wharves is especially likely to be heavily infested and this is the case even when scrupulous scavenger work renders its propagation at the spot impossible. The source of supply under such circumstances may be far removed and the fly population maintained by the constant arrival of individuals which accompany animals on their journeyings or which are guided by their sense of smell in independent flights from more or less distant localities.

The stable fly will breed in unmixed manure of horses and cattle, in such materials mingled with particles of straw and in rotting straw alone. While we have repeatedly bred the stable fly in large numbers from naturally infested, unmixed dung of horses and even a few individuals from that of cattle, the observations of Bishopp during a recent severe outbreak of the fly in north Texas, indicate that decaying straw is the material most favorable to its propagation. His careful work shows conclusively that in the order of preference, the substances in which *Stomoxys* will breed are oat, rice, barley, and wheat straw, horse manure, lot manure, and cow manure; that pure horse and cow manure are less attractive to the fly than when mixed with a considerable quantity of straw and that under a combination of conditions of plentiful moisture and abundance of rotting straw, breeding will occur at its maximum intensity.[13]

Similar observations have been made by Lucien Iches in Argentina.[14]

There is a direct relation between the presence and numbers of domestic animals and the abundance and distribution of this fly, which wanders far from its breeding places in search of food and will follow animals for long distances. This, however, is not its

[13] F. C. Bishopp, The Stable-Fly (*Stomoxys calcitrans L.*), Jour. Econ. Ent., 1913, vi, No. 1.

[14] Lucien Iches, *Stomoxys calcitrans L.* et le betail Argentin., Bull. Soc. nation Acclimat., France Ann., 1909.

only means of dispersion, as steamships, passenger trains, and those carrying live stock upon railroads are a common aid to its migration. We have encountered the species under all these conditions and have seen it carried for hours on the under side of an automobile top, in spite of wind and jolting over rough roads. In the latter case, the fly appeared to be full fed and, resting in this way after engorgement, it would be more likely to remain in such a situation and to be carried to a new locality. This is of special significance in connection with disease transmission. It is evident that flies carried in the ways mentioned, if infected or acquiring infection en route would have the power to carry the disease to a new locality remote from endemic foci. Particularly would this be the case if opportunity for feeding during the journey was lacking, as the hungry fly would upon arrival immediately seek a meal of blood, human or animal, and thus transmit the infection. An instance of the persistence of *Stomoxys calcitrans* in seeking blood was observed by us on the coast of South Carolina. The six occupants of a fishing boat were attacked, more than a mile from land, by numerous flies which suddenly appeared and which had evidently not been carried in the boat. It must be borne in mind that the stable fly is not attracted to offensive substances, and the odors from the fish-scented boat can hardly have played a part in drawing the flies so far from land. All the persons in the boat were bitten one or more times and the bare-legged boatmen greatly annoyed. They stated that such an occurrence was very common and that they were frequently attacked when at sea. *Stomoxys calcitrans* is very abundant along this line of seacoast and in the adjacent country. The day was clear and hot with a gentle off-shore breeze.

Although primarily a pest of live-stock, infesting and breeding in situations frequented by domestic animals, this fly often invades dwellings. While indoors it attacks the human inhabitants and we have even seen it more numerous in living rooms of mill dwellings than the ever-present house fly. It must be understood that in such cases the latter species was somewhat less numerous than usual.

Stomoxys has the habit of utilizing several hosts in order to secure a single meal, either from choice or because when dislodged by one host it flies to another.[15] This habit is important in connection with disease transmission. Especially is this the case in the interior of dwellings where all the members of the household would be exposed to the infection, if transmissible, which might be carried by one of its members.

It is, moreover, within the possibilities that a puncture of the

[15] C. T. Brues and P. A. E. Sheppard, The Possible Etiological Relation of Certain Biting Insects to the Spread of Infantile Paralysis, Jour. Econ. Ent., 1912, v, No. 4; Herbert Osborn, Insects Affecting Domestic Animals, Bull. 5, N. S. Bu. Ent. United States Dept. Agric., 1896; H. Maxwell-Lefroy, Biting Flies of India, 1907.

skin by an infected fly's proboscis might introduce the infection although no blood is drawn. This has been shown to be experimentally possible in the non-mechanical transmission of trypanosomiasis by *Glossina palpalis*.[16]

As has been pointed out, the members of the household who suffer most from pellagra are those who pass the most time in the home or its vicinity in the day time and it is these members, the females, who are most exposed during daylight hours to the attacks of *Siomoxys*.

As we have stated, *Stomoxys calcitrans* is not attracted by the odors of putrefaction. Hog-pens and privies are not inviting to it, nor is it apparently drawn to the nasal secretions of animals nor presumably to those of man as is the house fly, this discrimination being of importance in connection with the carriage of certain diseases.

FIG. 3.—A pasture provided by mill authorities for cows, etc. of operatives. Note cow-sheds hog-pens, and proximity of dwellings. The stream in foreground breeds *Simulium*

The stable fly is exceedingly abundant and generally distributed in Spartanburg County. In most of its geographical range the species is of importance in its relation to live stock and, our studies indicate, that it is also a pest of man with which it is necessary to reckon. No part of the region is free from this fly and it may be seen in numbers upon the streets of towns and villages, about barnyards, modest dwellings, and pretentious residences. Every

[16] A. D. Fraser and H. L. Duke, Proc. Roy. Soc., August 24, 1912, Ser. B, lxxxv, No. B, 581; Abs. Sleep. Sick. Bull, 1912, 4, No. 40.

team upon the roads is followed, and every cow in pasture or barnyard is constantly exposed to its attack during the daylight hours

As a part of the study devoted to this species, statements regarding its biting were obtained from as many persons as it was possible to interview, the questions being put to pellagrins and their families as well as to non-pellagrins. In obtaining reports on the biting habits of the fly, great care was exercised not only to be sure of the identity of the fly of which the individual was speaking, but to suggest nothing which might influence the tenor of the report. All reports were rejected which after careful consideration seemed doubtful, either as to the identity of the insect or the details of the statement.

Reports relative to the biting of *Stomoxys* were obtained from 227 pellagra patients and of these 115, or 50.7 per cent., gave positive histories of attacks and to these should be added 10 from members of families of pellagrins who could not themselves recall having been bitten. In 112 cases, or 49.3 per cent., the patient could remember no bites or was positive that none had been inflicted.

In addition to the above reports, many persons not included among our pellagra sufferers recounted experiences with the persistence of attack and voracity of the fly.

Close attention was given to the presence of the fly in such situations as would facilitate its attack upon the inmates of dwellings of all descriptions, that is, its presence or absence about the yards and premises, especially upon the outside of houses near open, unscreened windows, upon porches, and the interiors of dwellings. The distribution of the fly in the latter situation has some significance, and observations were made to determine its preference for different kinds of rooms.

Stomoxys was present about premises, yards, sides of house, or porch of the homes of 136 pellagrins, being abundant in 94 instances.

An illustration of the universal distribution of the fly was seen in a mill village which was studied with special care. This village contained 113 inhabitated buildings, including the company's store and office. Stable flies were found about 103 of these buildings and inside of several of them. It was found that the distribution varied somewhat, houses seemingly free from the flies at the time of our first visit would be infested at a later time, the reverse also being true. Nevertheless, there were few dwellings about which individuals could not be found at any time and it is to be assumed that they were present at all buildings more or less frequently.

For various reasons, it was quite often impossible to make a careful search of the interiors of pellagrous dwellings and conditions of weather, light, etc., were sometimes unfavorable to the presence of the flies at the time of inspection and made their discovery

difficult. Enough observations of its presence were made to show that invasion of human habitations is of common if not regular occurrence.

Its presence was noted in more than 30 dwellings of pellagrins, in fully half of which it was abundant, and in one instance a partial count showed 30 individuals.

The character of the rooms frequented by the fly has a bearing, not only upon the opportunity for attack, but upon its general habits. Strong preference was shown for the living rooms and in more than half of the houses studied these were the only rooms infested. In about one-fourth, flies were found in both living rooms and kitchen, while in only one instance was the kitchen alone infested and then by only one or two flies. In the houses of mill workers the living room is usually also a bed room. It will be seen that in case of illness or during moments of relaxation, the occupant of a bed in a *Stomoxys*-infested room invites the attack of the fly. It was evident that in addition to the odors of putrefaction, those of cooking are not attractive to this species, which is in strong contrast to habits of the house fly. The difference in domestic habitat of the two species is very striking, kitchens frequently swarming with house flies where living rooms were only moderately infested, the same houses showing infestation of *Stomoxys* in living rooms only.

Mangement of Live-Stock in Mill Villages, Etc. The relation of domestic animals, especially horses and cattle to the presence and abundance of *Stomoxys* is so important, that a knowledge of the number and management of these animals is essential to a study of the bionomics and distribution of house and stable flies.

Cattle, horses, mules, and hogs are very commonly kept in Spartanburg County especially upon farms, while in the cities, towns, and hamlets, many of the non-farming residents maintain milch cows and driving or draft animals. The inhabitants of the mill villages, also keep many cows, one cow to about three families being a fair average.

Upon farms, the stables and sheds in which animals are housed are usually placed about the barnyard at no great distance from the dwelling. Manure is often allowed to accumulate, and the floors of the outbuildings are frequently covered by a deep layer of droppings, the fresher portions heavily infested with fly larvæ. These conditions are by no means invariable and in many instances manure is not allowed to accumulate about the stable or barnyard, but is disposed of more or less promptly.

The definite allotment of land for purposes of pasturage is not invariable and, especially when but a few head of stock are maintained, they are pastured in a more or less indiscriminate fashion upon waste land, in lanes, woods, and such situations as prevent danger to growing crops. As a rule the milch cows are brought

to the barn to be milked, and draught-stock is invariably stabled and fed. Hogs are sometimes pastured but are frequently confined to small yards or pens which, too often, are unsanitary in the extreme and highly attractive to house and blow flies.

In cities and small towns, with the exception of the poorer dwellings, many, if not most, residences are provided with a stable in which a horse or cow, sometimes both, are sheltered. Depending somewhat upon density of population, these animals may be pastured upon vacant lots, road sides, and door yards or they may be confined to small yards adjacent to the stable. The care given the animals and their quarters varies greatly, but ample opportunity for fly propagation occurs. Hogs are usually excluded from the corporate limits of the larger communities.

In most of the mill villages there are no regulations regarding the keeping of domestic animals, including hogs. Cows are pastured indiscriminately about streets and village lots. They are stabled in small shacks upon the house lots of their owners or even under the houses when these stand upon sloping ground and sufficient room for this purpose is afforded. The cows are milked and fed grain, etc., on the premises, and their droppings are a source, sometimes a prolific one, of fly breeding.

In a few of the mill villages a common pasture is provided in which the cows of the mill operatives must be kept. They are not permitted upon the streets or house lots, and rough shed stables are usually provided in which the animals are fed, milked, and sheltered in inclement weather. These sheds are roughly constructed and although the droppings are removed from the stalls at intervals, piles of manure are left for varying periods in the immediate vicinity providing breeding places for great numbers of flies.

The plan of exclusion is an excellent one, but, unfortunately, the benefit is minimized by certain details of its application. Pastures are usually contiguous to the village, the nearest houses often standing within 100 feet of the pasture boundary and cow sheds. In one instance the pasture is almost at the centre of the village and is closely approached on three sides by the dwellings. In another village there are two pastures at opposite sides of the village and a large part of the community is thus exposed to the flies frequenting or produced within them. The rule of exclusion is not always rigorously enforced and exceptions are sometimes permitted; calves are occasionally, either openly or surrepticiously, kept about the owner's house and in one instance which came under our notice a cow was regularly brought for milking to the owner's house in spite of the regulation and an examination of the surroundings showed a large number of stable flies about the house adjoining that of her owner, whose premises were comparatively free from them.

A fact bearing upon the importance of domestic animals in connection with *Stomoxys* in its relation to human beings is that of

FIG 4.—Open commons used as cow pasture by mill operatives. The stream in foreground is an active *Simulium* breeding place. Houses of operatives in middle distance.

FIG. 5.—Part of a mill pasture with hog-pens and dwellings. Nearest house is about sixty yards from fence.

attack upon milkers. Although in the presence of animals which the fly normally prefers to man, the comparative quiescence of the persons so engaged, renders them peculiarly liable to attack, while those attending to and associating with cattle while actively engaged upon their duties may escape. That the milker is frequently attacked is shown by the reports we received.

But 21 pellagrins of our series had been in the habit of milking cows, and 2 of these were not questioned regarding the fly in this connection. Of the remaining 19, 14 or about 74 per cent., stated that they had been bitten while milking, and a considerable number of non-pellagrins made similar statements.

The comparative distribution of *Stomoxys* in urban, rural, and mill districts is interesting. Infestation of premises—the presence of *Stomoxys* upon the outside of houses, upon porches and in the immediate vicinity—in places from which entrance to the house or attack upon its inmates would be easy, occurred most frequently in mill villages. In these villages 97 per cent. of the homes visited were infested in the way described while of rural and farm homes 67 per cent., and of urban, 50 per cent. were similarly frequented.

The explanation of this seems to be that in the presence of domestic animals, the stable flies in the immediate vicinity will be concentrated upon and about them and many follow them when driven to work or to pasture, so that in the absence of the animals the infestation of the premises may be greatly lessened or the flies be so few as to escape notice. In the mill villages, the flies, separated from passing teams or cattle become generally distributed, seeking shelter and food among the dwellings, and it is significant of the truth of this explanation that in mill villages whose rules do not exclude cows from the village precincts, the number of stable flies present about the houses is more variable although apparently larger in the aggregate than in those villages which practice exclusion.

In comparing the reports of biting by *Stomoxys* received from pellagrins of the three classes, it is interesting to note that 55 per cent. of the reports received from mill cases were positive; 54 per cent. from rural cases were also positive; while but 13.4 per cent. of the urban cases could recall attacks by the fly.

It will be seen that the highest percentage of reports of bites by *Stomoxys* was received from the mill villages which also furnish the greatest number of pellagra cases. The rural districts follow closely in their percentage of positive reports though there is a greater discrepancy between pellagra incidence in the mill villages and that of these districts than is indictaed in the reports. This fact might be accounted for by the lack of congestion of population in the rural sections with a lower percentage of possibly infected flies.

These reports evidently indicate that there is a definite correlation

between the abundance of *Stomoxys*, the character of its distribution and its biting of man.[17]

SUMMARY. Our investigation was entered upon with no bias in favor of the infectiousness of pellagra or its transmissibility by insects. In the nature of the case, however, and as a basis for our work, it was necessary to assume that both were among the possibilities.

No preconceptions as to the involvement of any particular insect were indulged, and our conclusions regarding individual species of insects are based upon the epidemiological picture of pellagra, mainly as presented in Spartanburg County, and upon the habits and distribution of the insects as observed by us and as elsewhere recorded.

Ticks, lice, bed bugs, cock roaches, horse flies, fleas, mosquitoes, buffalo gnats (*Simulium*), house flies, and stable flies (*Stomoxys*) were under consideration. Of these, horse flies have nothing and cock roaches little to support them.

Ticks and fleas are excluded on account of their scarcity and the nature of their biting habits. In view of these characteristics, it is doubtful if even the existence of an animal reservoir of infection would bring the groups into prominence.

Lice and bed bugs do not account for the sex or age incidence or the rural nature of the disease; the scarcity of the former is an additional reason for its exclusion.

The rarity of mosquitoes here and the lack of coincidence between their distribution and that of pellagra for the State in general, together with the night-biting habits of the local species, which fail to account for the sex incidence, seem sufficient cause for their elimination.

House flies (*Musca domestica*) should be active if the malady is an intestinal infection in which the germ is passed with the feces, with contaminated food acting as the vehicle of infection.

The buffalo gnats (*Simulium*) should be eliminated, principally by the facts of their biting habits and lack of those of intimate association with man, also possibly by their comparatively moderate abundance (in our territory). We find that in Spartanburg County they are hardly known as a pest of man and when they do attack him, it is very locally and largely confined to field workers. Had Sambon's theory not been advanced, these flies could hardly have attracted suspicion of any connection with pellagra in this country.

The stable fly (*Stomoxys calcitrans*) displays certain salient characteristics which seem to qualify it for the role of a transmitter of pellagra.

The range of this one species covers and exceeds that of pellagra;

[17] Allan H. Jennings and W. V. King, One of the Possible Factors in the Causation of Pellagra. Jour. Amer. Med. Assoc., January 25, 1913, lx.

its seasonal activity, likewise, is coincident with that of the disease and, although its period of greatest abundance is somwehat later than the maximum intensity of pellagra, its appearance in spring precedes that of most of the spring recurrences and new cases, at which time it is already abundant; it is an abundant species, its abundance being most manifest in rural districts thus corresponding with the rural nature of pellagra, its numbers amply fulfilling our conception of those necessary to effective disease transmission; it bites by day only, thereby offering an explanation of the phenomenon of sex incidence and the related one of age distribution; it is intimately associated with man and habitually infests his vicinity and enters his dwellings; it bites man frequently and persistently; its longivity seems sufficient for the development of a hypothetical causative organism; it is readily and frequently carried long distances and might thus account for the occurrence of sporadic cases of the disease.

REVIEWS

SURGERY OF THE EYE, A HAND-BOOK FOR STUDENTS AND PRACTITIONERS. By ERVIN TÖRÖK, M.D., Surgeon to the New York Ophthalmic and Aural Institute; Ophthalmic Surgeon to Beth Israel Hospital; Consulting Ophthalmologist to the Tarrytown Hospital, and GERALD H. GROUT, M.D., Assistant Surgeon to the New York Ophthalmic and Aural Institute; Instructor in the Eye Department, Vanderbilt Clinic; Consulting Ophthalmologist to the Bellevue Hospital, First Division. Pp. 509; 509 illustrations, 101 in colors, and 2 colored plates. Philadelphia and New York: Lea & Febiger, 1913.

THE purpose of this work is primarily to give to the student a clear and detailed description of the steps of the operations necessary in the surgical treatment of diseases of the eye; in this the authors have succeeded admirably. Indeed, it is difficult to see how the descriptions could be improved upon. But the book is more than this. It sets forth briefly and clearly the surgical anatomy of the eyeball as a whole, and of the accessory structures before entering into a description of the individual operations. The different pathological conditions requiring operative interference are also clearly described and where there are several procedures for attaining the same end, the proper selection is indicated. Every step almost is illustrated by a diagram; inspection of the latter alone gives a fair conception of what is intended to be conveyed; the illustrations are of inestimable value to the descriptions.

The first chapter is devoted to considerations upon eye operations in general, such as the preparation of the patient, the operating room, illumination, preparation of instruments and dressings, anesthesia, postoperative treatment, and complications. A second chapter deals with the instruments, most of those employed being figured, many in their natural size; a list of the same covering two pages completes the chapter (armamentarium).

The surgical anatomy of the eyeball is exceedingly well described in the brief space of a short chapter.

As evidence that no operative procedure is considered too insignificant, we find minute directions for the removal of foreign bodies from the cornea, whether upon its surface or in the deep layers; the procedure to be followed in the case of foreign bodies which have partially penetrated into the anterior chamber (keratome passed into the anterior chamber behind the foreign body)

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is of course described. The localization and treatment of a foreign body within the eyeball and orbit is very properly compressed into a small space, as this part of ophthalmic surgery is quite a specialty in itself and requires special apparatus and training.

When considering operations upon the ocular muscles, whether resection or advancement, the authors appear to favor the former based upon "pathological examination of eyes after advancement which has shown that the advanced muscle becomes adherent to the sclera at its new insertion and the space intervening between this point and its old attachment. So it would seem that the advancing of the insertion of the muscle *per se* was of no value and the improvement obtained by the operation was due to a shortening of the muscle the same as in resection. The point of leverage in both cases is the original insertion of the muscle."

The writers make no comparison between the advantages of tenotomy and its opposite, which they entitle operations to strengthen the action of an ocular muscle, as against the former which is intended to weaken the same. Both types of operation are declared to be imperfect, as the final amount of weakening or strengthening can never be foretold in either case, this being particularly true of tenotomy. Operations in heterophoria are said to be indicated only in high degrees, when other measures fail to give relief. We readily draw the inference that the authors are no advocates of partial graduated tenotomies in heterophoria. We find no reference to orthoptic training in strabismus and this perhaps quite properly, as the latter is not a surgical procedure.

In the treatment of diseases of the lacrimal passages, Toti's operation is well spoken of upon the basis of satisfactory personal results. Probing, styles, and stricturotomy are not recommended. The indications for extirpation of the sac are given, but comparison with Toti's operation is not made. Lagrange and Elliott's operation are described in the treatment of glaucoma, as is also Heine's method of cyclodialysis. The theory of the latter seems to be faulty upon the basis of anatomical examinations which showed that the ciliary body had become firmly reattached to the overlying sclera.

To the operations for cataract as is natural, is given the most space. The descriptions are excellent and leave little to be desired. We have not found any reference to Smith's Indian operation, with the exception of eight words in the description of the anatomy of the lens, where it is stated that the capsule is left behind in the operation for cataract "unless the lens is extracted in the capsule."

Dr. Arnold Knapp in the short introduction to this work makes the statement "that the authors have succeeded admirably in their project." The reviewer heartily endorses this opinion.

The publishers' work is well done. The type, paper, and press-work leave nothing to be desired. T. B. S.

CYCLOPEDIA OF AMERICAN MEDICAL BIOGRAPHY. By HOWARD A. KELLY, M. D., Professor of Gynecologic Surgery at Johns Hopkins University, Baltimore. Vol. I: Pp. 509; 10 portraits; Vol. II: Pp. 545; 24 portraits. Philadelphia and London: W. B. Saunders Company, 1912.

No more servicable addition to the literature of American medicine has been made in recent years than Dr. Howard A. Kelly's monumental work on American medical biography from 1610 to 1910. The labor involved in compiling the two volumes which comprise this work has been enormous, and we indeed owe a debt of gratitude to the man whose energy and enthusiasm prompted him to undertake such a stupendous task. As a result of his zeal we possess what has been much needed, an up-to-date and complete, yet convenient biographical cyclopedia.

The greater part of the two volumes consists of a series of short biographical sketches alphabetically arranged. These sketches give a brief outline of the lives of twelve hundred distinguished medical men who have lived and labored in the United States and Canada during the past three hundred years. The completeness of the list is surprising, and omissions, if there are any, must be few, for the names given include all who have been conspicuous as investigators, writers, teachers, and leaders in medicine and the various medical sciences on this continent. For one man to write such an array of biographical notes would have been well nigh impossible. Dr. Kelly therefore, wisely associated with himself a group of collaborators who were particularly interested in work of this kind. Their names are mentioned in the preface and their initials appear under the sketches that each has written. The result of this method is a collection of biographies that are bright, interesting, and sufficiently varied in style to prevent the monotony which is too apt to pervade books of this type.

The most interesting part of the work is a series of nine able introductory articles describing the development and progress of the various medical specialities in America, namely: Anatomy, surgery, gynecology, obstetrics, ophthalmology, laryngology, medical jurisprudence, army and navy, and women in medicine. These articles take on an added value and authority from the fact that they have each been contributed by a separate author who in every instance is well qualified to perform the task. Happily the subjects of gynecology and obstetrics have been written by Dr. Kelly himself.

The numerous portraits of particularly well known and distinguished medical men that appear throughout the book, add considerably to the beauty and interest of the work.

The enthusiasm with which the work will undoubtedly be received throughout the country should assure Dr. Kelly that his

years of painstaking effort in the preparation of this book have met with the full appreciation of his colleagues and of all who take pride in the long list of tireless and hardy workers whose names will ever be associated with the advances and triumphs of American medicine. G. M. P.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M. D., Professor of Therapeutics and Diagnosis in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital, etc. Assisted by LEIGHTON F. APPLEMAN, M. D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia, etc. Vol. II, June, 1913; pp. 449; 131 illustrations. Philadelphia and New York: Lea and Febiger, 1913.

MANY interesting volumes of *Progressive Medicine* have been reviewed in these columns, but none has furnished more instructive and important information than is to be found in Volume II for this year, which has been recently published. The opening contribution of 67 pages by William B. Coley deals exclusively with hernias, the many and varied phases of which are carefully discussed. John C. A. Gerster follows this with an admirable article of 118 pages on recent advances in surgery of the abdomen, exclusive of hernia. Under the stomach he dwells at length upon recent important observations on the Röntgen ray diagnosis of various gastric conditions and upon gastric ulcer. The small intestine, appendix, and large intestine are next discussed. Under the latter his views on the surgical treatment of constipation, with special reference to the notable work of W. B. Cannon and Arthur Keith on the anatomy and physiology of the large bowel, and Coffey's work on gastro-intestinal stasis and ptosis are well worth careful study by both internist and surgeon. Under the head of the liver, bile passages, and portal vein Gerster not only deals with a number of surgical considerations, but also invades the realm of medicine to the extent of devoting four pages to Roger's emetine treatment of amebic disease.

John G. Clark furnishes his always interesting review of gynecology. Very properly a little over one-quarter of his 116-page contribution is devoted to the cancer problem. Almost as much space is given to a discussion of Röntgen therapy in gynecology, especially in reference to uterine myomas. Uterine malpositions, menstruation, the ovary, gonorrhea in the female, tuberculosis of the kidney, cystitis and urethroscopy, and sterility in women may be mentioned specifically from among the many other important subjects upon which he lays stress.

The medical section of the volume consists of Alfred Stengel's 120-page article in which the various elements of the blood, including the bone marrow are first discussed. Pernicious anemia is disposed of in a few pages, whereas 18 pages are devoted to leukemia, indicating the trend of investigation during the past year. Primary splenomegaly and polycythemia are also dealt with at some length, as is hemorrhagic disease. After a brief survey of the adrenal glands and their diseases, Stengel devotes about six pages to gout and then enters upon a careful consideration of recent work on diabetes. Somewhat over a fourth of his entire contribution is given over to a discussion of the thyroid gland, various conditions affecting it, and exophthalmic goitre in particular.

In a short review of some 30 pages on ophthalmology, Edward Jackson contributes the concluding section. Under the various anatomical divisions of the eye he takes up the contributions of importance that have appeared during the past year in this particular field of work. G. M. P.

THE CATARRHAL AND SUPPURATIVE DISEASES OF THE ACCESSORY SINUSES OF THE NOSE. By ROSS HALL SKILLERN, M.D., Professor of Laryngology, Medico-Chirurgical College, Philadelphia. Pp. 389; 247 drawings and 5 colored plates. Philadelphia: J. B. Lippincott Company, 1913.

As he states in his preface to this able work, the author has endeavored to present in the English language a comprenhesive and complete text-book on the nasal accessory sinuses. Heretofore the student of the many problems inspired by the vast interest in this subject that has arisen in recent years, mainly through the researches of the German school, has been compelled to seek for information in the works of Hajek, Zarnico, and others in German, or Luc in French. The only work in English dealing extensively with nasal sinusitis has been that of Logan Turner, of England.

The present volume bears ample evidence of the great amount of work and painstaking care of the author as shown by the references, well arranged at the foot of each page, there being no less than 586 of these, comprising an almost complete bibliograph of the subject.

The work is systematically arranged for convenience in study and reference, starting with a chapter on general considerations, which includes anatomy, physiology, differential diagnosis, and treatment. The four succeeding chapters deal with the respective sinuses in detail, namely, the maxillary sinus, the frontal sinus, the ethmoid labyrinth, and the sphenoid sinus. The plan in each of these is to give the detailed surgical anatomy, etiology, diagnosis, symptoms,

technique of the different procedures necessary for diagnosis and treatment and lastly the surgery, intra- and extra-nasal.

Of the many unique and admirable features of the book one can only mention a few, but the first point that impresses the reader is the number and quality of the illustrations by such well-known artists as the Fabers. Almost all of these are original, being made from the author's own anatomical preparations and are drawn strictly to illustrate the text. As an instance of this, no less than seven large drawings from photographs depict every step of Dahmer's operation on the maxillary sinus with such clarity that a novice must understand; six show the preturbinal method; six the Caldwell-Luc; while ten are required to amplify the description of the Killian operation on the frontal sinus. These are merely the most striking instances of a feature that adds greatly to the merit of the work. But by no means are all the illustrations of operative procedures; many excellent anatomical and pathological drawings being included.

It is well known to any student of the sinuses that more variations exist in the bony structure and arrangement of these cavities than in any other part of the body and it is this that lends interest to the study, as well as difficulty and uncertainty in treating their diseased conditions.

Many of these anomalies are shown, taken from specimens of the author and others, and every endeavor is made in the text to guard the operator from being misled. The descriptions are systematic and clear and every phase of the subject is covered; so thoroughly in fact that it is distinctly a text-book for the specialist rather than for the general practitioner.

As the first American work on the subject it should appeal to all those practising the specialty of rhinology and should be almost equally valuable to the ophthalmologist, and is not out of place in the library of the up-to-date internist. G. M. C.

INSOMNIA: ITS CAUSES AND TREATMENT. By SIR JAMES SAWYER, of London, Doctor of Medicine of the University, Fellow of the Royal College of Physicians. Second edition; pp. 107. Birmingham: Cornish Brothers, 1912.

THIS small book consists of the first three chapters of the author's "Contributions to Practical Medicine," fifth edition, 1912, and is published separately for the convenience of the profession.

This volume makes delightful reading. In the first chapter the causes of insomnia are discussed and the usual theories given. The second and third chapters are the important ones. In them treatment is discussed by drugs, exercises, general methods, psychic treatment,

etc. Besides there is a useful summary at the end. In a word, this small volume is full of good practical suggestions based upon sound logic and experience. It is delightfully written and contains references to the foibles of some of our celebrities. Accordingly, to induce sleep beer was used by Lord Bacon, while King George III slept with his head on a hop pillow, and even King Edward VII was addicted to this. Charles Dickens' plan was to stand at his bedside until he felt chilly, and then hop into bed and go to sleep, and the illustrious William Harvey was in the habit when he was "hott-headed" and his thoughts stirring to such an extent that they would keep him from sleeping, of arising out of bed and walking out of his chamber in his shirt until he began to shiver, and then would return to his bed and sleep comfortably. T. H. W.

THE COLLECTED WORKS OF CHRISTIAN FENGER, M.D., By LUDVIG HEKTOEN, M.D., Professor of Pathology at Rush Medical College. Two volumes; averaging 525 pages each, illustrated. Philadelphia and London: W. B. Saunders Company.

AMERICAN surgery owes much to Christian Fenger. His work in applying the knowledge of pathology and pathological anatomy to the furtherance of surgery was pioneer in this country. He also was one of the first to embrace the principles of Lister and to point out the great advantage in results to be obtained by those methods. These volumes represent the praiseworthy effort to preserve in memorial form the collected writings through the medium of which so great an impress was made upon his contemporaries. The breadth of his interest may be seen by a cursory perusal of the titles of the 75 papers which embrace almost every branch of surgical practice.

Many of the contributions may be recommended as models of scientific writing in that the conclusions are based upon an orderly array of evidence carefully gathered, thoroughly digested, and simply presented. The collection is of historical value and of special interest to those whose fortune it was to have been associated in any way with the gifted and stimulating author. D. B. P.

DISEASES OF THE EYE. A MANUAL FOR STUDENTS AND PRACTITIONERS. By J. HERBERT PARSONS, D.Sc., M.B., B.S., F.R.C.S. Second edition. Pp. 684; 328 illustrations. Philadelphia: P. Blakiston's Son & Co., 1912.

IN the second edition of Parson's *Diseases of the Eye* the author has revised the text, adding several new sections, and has intro-

duced additional illustrations and colored plates. The book is one of the best of the moderate-sized manuals on diseases of the eye, and is readable because of its simplicity and directness of style Especially to be recommended as of value to the student are the sections on physiology and elementary physiological optics. There are 17 full-page plates, all but two of which are colored. The productions of fundus conditions are notably good, much better than those in many more pretentious text-books, especially in those published in America. Despite the fact that Mr. Parsons' writing has been largely in the domain of ocular pathology, this portion of the subject has not been allowed to overshadow the others, and the clinical descriptions are good. Treatment, especially from a constitutional viewpoint, is perhaps too briefly considered, but those who wish to pursue the subject more deeply are referred to Fuchs' text-book, and for treatment to Hanke's *Treatment of Diseases of the Eye*, which was translated by Coats and the author. Three appendices are given; one containing a method for preliminary investigation of the patient, the second therapeutic notes, and the third, the requirements for admission into the public services. On the inside of the back cover is a set of Holmgren's wools for color blindness. It is pleasure to cordially recommend the volume. E. A. S.

THE TECHNIQUE AND RESULTS OF RADIUM THERAPY IN MALIGNANT DISEASE. By M. DOMINICI, M.D., Paris, Chef du Service de Pathologie Interne, Laboratoire Biologique du Radium, and A. A. WARDEN, M.D., Glasgow and Paris, Visiting Physician to the Hertford British Hospital. Pp. 29, with 24 illustrations. Philadelphia: P. Blakiston's Son & Co., 1912.

THIS is a reprint from a report published in the *British Medical Journal* of August 27, 1910, of a clinical demonstration given by Dr. Warden for Dr. Dominici before the British Medical Association in 1910, with additional notes on the cases up to March, 1912. The report covers the results obtained by radium treatment of 9 cases of growths of a serious nature that were either inoperable or in which operation was declined. Reproductions from photographs of several of the cases are presented, showing the appearances before treatment and the admirable and really remarkable results obtained. Some of the reports are accompanied by reproductions of micro-photographs of sections of the growths made before and during the progress of treatment. H. K. P.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

CHIEF OF THE DEPARTMENT OF INTERNAL MEDICINE, CLIFTON SPRINGS SANATORIUM AND HOSPITAL, CLIFTON SPRINGS, NEW YORK.

The Experimental Prodution of Typhoid Bacillus-carriers in the Rabbit.—UHLENHUTH and T. MESSERSCHMIDT (*Deutsch. med. Woch.*, 1912, xxxviii, 2397) refer to the importance of bacillus-carriers in the spread of typhoid fever. As the gall-bladder is so frequently the depot of infection, it has been opened and drained in a number of instances, but the result is not always successful. By vaccine treatment uncertain results are also obtained; the bacilli disappear, only to reappear in a few months, as Uhlenhuth and Messerschmidt have been able to demonstrate. Chemical agents, such as chloroform, xylene oil, and potassium iodide, have likewise failed to inhibit the growth of the bacilli. The experimental therapy of bacillus-carriers cannot be properly undertaken until the conditions in man are reproduced in laboratory animals. By direct inoculation of the gall-bladder of rabbits, Uhlenhuth and Messerschmidt have succeeded in producing chronic bacillus-carriers experimentally. After six months the bacilli were still present in the gall-bladder. Such animals have been employed for experimental therapy; Uhlenhuth and Messerschmidt attempted immunization by vaccine and also employed chemical agents. By previous injection of vaccines they found it impossible to prevent the growth of typhoid bacilli in the gall-bladder of rabbits. Furthermore, rabbits which had been made chronic bacillus-carriers could not be cured by subsequent vaccination. Next, they employed a series of chemical substances but also without result. The substances used were iodethylhexa-methylentetramine, a mercury-atoxyl derivative, salicylate of copper, neosalvarsan, salvarsan, phosphorus, and colloidal mercury. Uhlenhuth and Messerschmidt found that the inflammatory changes in the gall-bladder of the rabbit were similar

histologically to those found in man. Occasionally they found that animals inoculated in the gall-bladder became sick and died with signs resembling those of typhoid fever in man, both clinically and anatomically. By reproducing the condition in animals, they have opened the way for a rational experimental therapy of typhoid bacillus-carriers.

On the Presence of Diphtheria Bacilli in the Urine.—R. Koch (*Deutsch. med. Woch.*, 1912, xxxviii, 2356) has not found diphtheria bacilli in the urine of patients suffering with diphtheria as frequently as did Comardi and Bierast, who reported their presence in 54 of 155 cases. Koch examined 111 specimens of urine from 26 patients, and in 4 of these specimens from 2 patients he was able to cultivate organisms which were virulent when tested experimentally. In 10 other specimens from 5 patients suspicious organisms were cultivated by Loeffler plates, but it was either impossible to cultivate them in pure culture or they proved avirulent to animals. The virulent organisms were obtained in each instance from patients who died in the early stages of the disease from paralysis of the heart and vessels. Organisms similar to the avirulent diphtheroid bacilli were found in the urine 4 times out of 19 examinations of the urine of patients suffering with scarlet fever.

The Excretion of Formalin in the Urine after Hexamethylenamin (Urotropin).—Making use of the test for formaldehyde reported by Burnam, Talbot and Sisson (*Boston Med. and Surg. Jour.*, 1913, clxviii, 485) examined 400 specimens of urine from 44 children. Practically all the acid urines contained formaldehyde, and the alkaline urines were negative. This was after hexamethylenamin by mouth. All of the 44 children tested showed formaldehyde in the urine at some time, while under observation. Hexamethylenamin is often excreted as such by children in alkaline or neutral urine, and is almost never broken down into formaldehyde, except in an acid urine. In some cases the dose had to be increased before formaldehyde appeared. Relatively large doses are frequently necessary. Inasmuch as the antiseptic power of urotropin depends upon the presence of free formaldehyde, urotropin should not be given with drugs that cause the urine to turn alkaline.

The Excretion of Formalin in the Urine.—Smith (*Boston Med. and Surg. Jour.*, 1913, clxviii, 713) believes from observations that Burram's test for formaldehyde in the urine is simple and accurate. It is definitely positive when formaldehyde is present in the strength of 1 part in 40,000 or more. A negative test at one time does not prove that formaldehyde is never liberated, after hexamethylenamin by mouth. The formaldehyde is liberated by the acids of the urine, not by a specific function of the renal epithelium. The process may take place in the kidney but is continued in the bladder. The degree of acidity of the urine, as measured by its hydrogen ion concentration, showed a constant relation to its power to set free formaldehyde. The higher the acidity, the greater was this power. In cases with persistently alkaline urine, Smith tried to change the reaction with

various drugs. Sodium benzoate, grains 15, t. i. d., had no appreciable effect; boric acid, grains 10, t. i. d., was effectual in several cases, but it is said to be toxic. Sodium acid phosphate given immediately after meals in ½- to 1-dram doses seemed more efficient than the other two, but may cause diarrhea. Among the fifty individuals whose urine was examined, there was only one case in which formaldehyde was never detected. As to dosage of hexamethylenamin, Smith feels that 5 grains does not lead to the appearance of formaldehyde in the urine, with enough regularity to warrant its routine use. Seven grains are followed by good quantities of formaldehyde lasting for six to ten hours. Ten grains every eight hours or 15 grains twice a day is the dose recommended.

Gastric Juice in Malignant and Non-malignant Diseases of Stomach and Duodenum.—SCHRYVER and SINGER (*Quarterly Jour. Med.*, 1913, vi, 309) conclude that there are no pathognomonic signs available in the gastric juice. No type of gastric juice is the exclusive or invariable accompaniment of any clinical condition. However, systematic gastric analysis helps to throw light on a number of pathological conditions. In the analyses Schryver and Singer, after a critical review of various indicators and methods, made use of the following: (1) For free hydrochloric acid: Dimethyl titration, appreciating that absence of dimethyl acidity may be due to either true achylia or a combination of secreted hydrochloric acid by amino-acid groups. (2) For "secreted" chloride: Substraction from the total chloride of the chlorine determined in the ash after incineration (separation of the chlorine as hydrochloric acid and in combination with organic substances from the chlorine as sodium chloride). (3) For the peptic activity: The method of Fuld-Levison, apparently proving that pepsin secretion can be influenced independently of the hydrochloric acid secretion. (4) For the "nitrogen factor": The proportion of the difference between the titration value with phenolphthalein and that with dimethyl to the amount of nitrogen present as amino-acids, multiplied by ten. (In estimating the acidity of gastric juice to indicators, the amount of nitrogen present must be taken into account. In healthy gastric juice the "nitrogen factor" tends to approximate to figures 2.4. It seldom falls below, but with diminution of the digestive power it may rise greatly above. Schryver and Singer feel from their application of these tests that "secreted chloride" (*i. e.*, total chloride less inorganic chloride) is the best available index of gastric efficiency as regards hydrochloric acid. The latter, as it is secreted, enters either partly or wholly into combination with the products of digestion. The amount combined depends upon the amount and character of these products, index of which is furnished by the nitrogen estimations and the determination of the "nitrogen factor." In uncomplicated cases of duodenal ulcer, the amount of "secreted chloride" is raised, together with the peptic index, while the nitrogen factor approximates 2.4. The pyloric ulcers resemble these in general characteristics. Carcinoma of the stomach has no specific effect on the composition of the gastric juice, although both pepsin and chloride readings are generally lower than in other conditions. In alcoholism the peptic index is depressed, while the chloride

secretion remains normal. With visceroptosis and nephroptosis there is a general depression of the gastric functions. The "nitrogen factor" is raised. The same conditions prevail with atonic gastric wall. Hyperchlorhydria, hypochlorhydria, and even achylia are encountered independently by coarse gastric lesions. The coincidence of definite hyperchlorhydria with a greatly raised peptic index is practically diagnostic of pyloric and duodenal ulcer among gastric diseases. Very low chloride readings practically exclude pyloric or duodenal ulcer. A "nitrogen factor" of 2.8 and over has been found to be almost diagnostic of delayed emptying of the stomach. Dissociation of chloride and pepsin secretion is probably the result of chronic inflammatory change in the gastric mucous membrane.

Amylolytic Ferments in the Urine.—CORBETT (*Quarterly Jour. Med.*, 1913, vi, 351) has applied Wohlgemuth's method of quantitative estimation of amylolytic ferments in the urine to a variety of conditions. Normal individuals secrete a starch-reducing ferment in the urine, in the fairly constant amounts of 10 to 20 units on the average. Each unit represents 1 c.c. of 0.1 per cent. starch solution converted into dextrine in one-half hour by 1 c.c. of urine. A diet containing starch will increase the normal amylolytic ferment content of the urine. This was striking in the change from a milk diet to one containing much carbohydrate. Normal blood serum, by an equivalent method, showed the presence of the ferment with an average value of 10 units. As a direct measure of renal efficiency, Corbett emphasizes leakage of ferment requiring no renal activity for its elimination, and considers the relation of the serum-content to that of the urine of greater value than the urine content alone. When the value of the serum constantly exceeds that of the urine, it may be assumed that there is a considerable loss of renal efficiency. High readings in the urine were never found in pure cases of renal disease. All the cases of undoubted pancreatic disease, whether malignant or inflammatory, gave high values, and Corbett recommends the test as an aid in diagnosis of these conditions.

Effect of the Antityphoid Serum of Besredka upon the Course of Typhoid Fever.—The remarkable anti-endotoxic action of the serum of Besredka has been demonstrated. Even 9 fatal doses of endotoxin have been neutralized by a certain dose of serum. ANDRIESCU and CINCA (*Annales de l'Inst. Pasteur*, 1913, xxvii, 170) have studied the effect of the serum upon the course of typhoid fever, particularly upon the elimination of typhoid bacilli. The question was especially interesting to them as the mortality in Roumania varied from 10 to 20 per cent. compared to 6 per cent. of carriers. They chose 17 cases of typhoid from among the more serious types. In each instance they verified the diagnosis by hemoculture and Widal reaction. Serum was given subcutaneously in three or four consecutive doses, 40 to 500 c.c. in total amount. Two cases received serum intravenously. The serotherapy was in addition to the classical treatment of baths, intestinal antiseptics, liquids in quantity, etc. With one exception, a fatal case, they observed evident improvement in the general condition, but no definite effect upon the temperature. The most striking

result was the disappearance of typhoid bacilli from the circulating blood even twenty-four hours after the injection of serum. The effect was more marked after intravenous than subcutaneous injection. This fact certainly means an intense bacteriolytic action of the serum. To Andriescu and Cinca this alone justifies the use of the serum, and is of first importance in solving the question of carriers.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Experimental Contribution to the Pathogenesis of Acute Hematogenous Osteomyelitis.—DUMONT (*Deutsch. Zeitschr. f. Chir.*, 1913, cxxii, 116) says that it is possible to produce in young, growing rabbits, without trauma, by the intravenous injection of staphylococcus cultures, an acute hematogenous, suppurative osteomyelitis. The clinical picture will correspond to that occurring in man from the same affection. The cultures must have a hemolytic effect on rabbit's blood. For the production of a focus of osteomyelitis, cultures of the Staphylococcus pyogenes aureus as well as those of the Staphylococcus albus, may be employed. The variety of the organism employed is not of importance. It is merely the virulence which is of importance. The statement that a specific cause of suppuration, the bacillus of osteomyelitis exists (Hencke), is based upon error. Dumont's experiments, in which he produced osteomyelitis with the Staphylococcus albus developed from other sources of infection than osteomyelitis alone, proves sufficiently the error of this hypothesis. He believes that his experiments have succeeded in proving, experimentally, the interpretation of Lexer of the etiology of acute hematogenous osteomyelitis. Lexer supported it upon the basis of the anatomical arrangement of the bloodvessels of the bone and the biological properties of the staphylococcus. At the site of their deposit in the finest capillaries, chiefly in those of the metaphysis, these increased in number and thus became a focus of suppuration.

A New Method for the Diagnosis of Renal Tuberculosis.—BUERGER (*Jour. d'Urolog.*, 1913, iii, 431) says that he has demonstrated that the excision of a portion of the mucosa from the meatus of the ureter, can show the presence of miliary tubercles at a period when all other

evidence of renal tuberculosis is absent. Miliary tubercles may be present in this tissue, when the only visible change in the mucous membrane, even for the trained eye, is the appearance of "edema." The excision of this portion of the mucous membrane permits a positive diagnosis to be made, when it is impossible to use the ureteral catheter, when inoculations into lower animals prove negative, when the urine is completely clear, and when the disease presents practically no symptoms. In the beginning of the disease, in questionable cases of renal tuberculosis, a tuberculous focus can concentrate and localize itself at the meatal orifice of the ureter. Miliary tuberculosis may be found in the ureteral ostium even when the rest of the ureter is scarcely affected by tuberculous lesions and also when the pelvis of the kidney is only slightly affected. It will be necessary to practice this method of diagnosis when the objective findings are sufficient to permit one to suppose the development of a renal tuberculosis. It should be resorted to also when one fails to find the tubercle bacillus, and always when positive signs of invasion of the kidney by the tuberculous process are absent.

A Note on the Surgical Treatment of Calculus in the Lower End of the Ureter.—LEMOINE (*Jour. d'Urolog.*, 1913, iii, 441) did a transvesical operation for a ureteral calculus, which by the cystoscope and *x*-rays had been located at the vesical orifice of the right ureter. A mild Tredelenburg position was employed and the ureteral meatus was widened by a longitudinal incision. The calculus, however, could not be located. Then an iliac incision was made and the ureter exposed subperitoneally. It was found dilated to the size of the small intestine, and was progressively denuded to the kidney, which, as well as the pelvis, was distended in proportion to the rest of the ureter. Finally the calculus was located in the upper pole of the dilated kidney. Because of the pus in the urine and the thinness of the renal wall, the kidney and ureter were removed. The patient recovered. The calculus was 3 cm. long, 2 cm. wide, and 12 mm. thick, and weighed 13 grams. To determine whether the stone is movable or fixed, several methods may be employed: (1) Repeated skiagraphs may be made at intervals of several days, in varying grades of the Trendelenburg position. Change in the position of the stone in the different skiagraphs, indicates its mobility. (2) The ureteral catheter may be arrested and thus indicate fixation of the stone. But this method is open to error because a stricture or spasm of the ureteral muscle would produce the same result, or the catheter may pass to one side of the stone. (3) A skiagraph taken with the arrested catheter in position would show them both, and thus give strong presumptive evidence of fixation of the stone. Various methods of dislodging a fixed stone are mentioned. It may be approached for removal by the vaginal, rectal, perineal, or sacral paths, but these are not often employed. The transvesical and the subperitoneal are the paths usually chosen. When the stone is recognized to be movable, one may by endovesical methods try to provoke its spontaneous expulsion, or by inverting the patient, cause it to pass to the kidney, where it can be removed by pyelotomy.

Calculi in the Intraparietal Portion of the Ureter.—PASCUAL (*Jour. d'Urolog.*, 1913, iii, 147) says that calculi in the inferior extremity of the ureter have a characteristic and special symptomatology. They manifest themselves above all by vesical symptoms which lead one to think that the patient is suffering from cystitis. The cystoscope, generally, shows a ureteral orifice surrounded by edema. The skiagraph and ureteral catheterization will show with certainty the seat and size of the stone. The removal will be made by the natural path when that is possible, or by the suprapubic route if extraction by the natural path is impossible or has failed.

Consecutive Displacement of the Cerebral Hemisphere in the Localization and Removal of Intracerebral Tumors and Hemorrhages (Apoplectic Hemorrhages and Clots).—HUDSON (*Annals of Surgery*, 1913, lvii, 492) reports the case of a man, aged forty-five years, who had been in the hospital two weeks, with a slight paralysis of the right side, which had slowly progressed during this period. Hudson was called hurriedly at 2 P.M. On the previous day the patient had suddenly raised himself in bed, after which he grew worse with the symptoms of an intracerebral hemorrhage. He was entirely unconscious during the night. An operation was begun at 2.30 P.M., one-half hour after Hudson was first called, without ether. Oxygen would have been administered, but breathing had failed and artificial breathing was attempted. The brain was rapidly and freely exposed in the parieto-occipital region. An immediate backward displacement of the brain was observed; and the patient began to breathe. A hurried palpation of the brain showed a point which appeared more promnient than any other. Through this point the dura was incised, when immediately the cortex in the apex of a convolution ruptured; several clots of blood and a quantity of fluid blood were forcibly thrown out. At this point the patient's condition had so improved that more deliberation was possible. The hemorrhage from the cavity in the brain was quite profuse, but was eventually controlled with bits of dry cotton. The dura was not closed, and the finger of a rubber glove was caught with a stitch of fine catgut in the lower border of the dura. The brain at this point occupied its normal position within the dura, the abnormal tension produced by the hemorrhage having apparently disappeared. The bone flap was closed down and the scalp closed, the rubber drainage being brought out through an original trephine opening in the skull and the original incision in the dura. The hemorrhage was rather free for three or four days, and continued until the eighth, necessitating daily changes of dressing. The patient rapidly recovered, and was walking about the hospital from the fourth to the twelfth day, when he left. It is Hudson's belief that the surgery of the brain, which is the tap root of the tree of surgery, has failed to advance because of the surgical tools by which this surgery was attempted being inadequate for this work. He further believes that, with the thorough understanding and the proper application of this means, and by observing these methods of doing cranial surgery, the purely mechanical procedures are rendered as easy, quick, and safe as in abdominal surgery.

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THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Treatment of Pernicious Anemia.—BRAMWELL (*British Med. Jour.*, 1913, 2734, 1093) reports the results in 11 cases of undoubted pernicious anemia and in 1 doubtful case treated by salvarsan. Of the 11 undoubted cases, 4 have been apparently completely cured, but it is impossible to say whether a relapse will occur later or not. In 2 cases there was very striking temporary improvement, but ultimately they relapsed and death resulted. In 1 case there was slight improvement at first, but the patient died from bronchopneumonia while under treatment. In 2 cases there was no improvement, and in 1 case still under treatment there is slight improvement. Bramwell has had nearly forty years' experience with the ordinary arsenical method of treatment of pernicious anemia, and he believes that the salvarsan treatment is superior to the ordinary arsenical treatment. Further experience is necessary, however, before one can say whether the beneficial effects, which it undoubtedly produces in many cases, will be lasting or merely temporary. Bramwell has always given the salvarsan intramuscularly, the dose used being 0.3 gram, which is half the dose usually employed in syphilis. In view of the fact that pain and inflammation often follow intramuscular injections of salvarsan, he advises neosalvarsan, which does not produce such marked local reactions.

The Treatment of Diabetes with Rectal Injections of Sugar Solutions.—LUTHJE (*Therapie der Gegenwart*, 1913, liv, 193) reports good results from the administration of glucose solution to diabetics by rectal injection by the drop method. He says that the sugar is much better absorbed and utilized by diabetics when given in this way than when given by mouth. He has had especially good results in the treatment of acidosis by this plan. By the drop method, most persons can absorb from the rectum from one to two liters of fluid a day. He uses a 5.4 per cent. glucose solution, and hence the amount of sugar absorbed would be from 50 to 100 grams a day.

A New Protective Measure against Diphtheria.—VON BEHRING (*Deutsch. med. Woch.*, 1913, xxxix, 873) reports in detail his new method of active immunization against diphtheria. His preparation is a mixture of very strong diphtheria toxin and antitoxin combined in such proportion that the mixture shows only a slight, if any, surplus of the toxin when tested on guinea-pigs. The ordinary prophylactic measures against diphtheria have proved to be ineffectual and von Behring believes that this preparation is more efficient in producing

immunity against diphtheria than diphtheria antitoxin alone. He believes that one or more inoculations of his preparation will produce a protracted immunity to diphtheria and he reports cases that seem to support his views.

The Therapeutic Use of Strophanthin.—THORSPECKEN (*Deutsch. Arch. f. klin. Med.*, 1913, cx, 319) advises the intravenous injection of strophanthin in chronic cardiac insufficiency where other remedies are ineffectual or when gastro-intestinal disturbances prevent the use of the ordinary cardiac stimulants. Strophanthin is especially indicated in failure of cardiac compensation associated with congestion of liver and in contracted kidneys associated with dyspnea or edema of the lungs. Thorspecken advises the use of an initial dose of one-half of a milligram and twenty-four hours later a second dose of three-fourths of a milligram.

An Attempt to Interpret Present-day Uses of Vaccines.—SMITH (*Jour. Amer. Med. Assoc.*, 1913, lx, 1591), in conclusion, briefly summarizes the points to be emphasized in his article. He says that all parasites tend to increase the resistance of the host in which they live and multiply. Out of this universal fact a number of practical problems arise. In any given disease is it worth while to try to raise this immunity, and how much energy will it cost the patient? If worth while, what is the best and most sparing way of raising such immunity artificially? In any localized infection we must ask: Is this a beginning process without attendant immunity, or is it a residual process associated with general immunity? If the latter, vaccines may be considered safe. In processes associated with fever and bacteriemia, science says "hands off" until we know whether we have a progressive disease with gradual undermining of the resistance, or a more localized affection in which the excursions into the blood are secondary. In any case the use of vaccines in these cases must be regarded as experimental, and should not be undertaken save in conjunction with one trained in immunologic problems. Judged from this point of view as well as from the work of the laboratory as a whole, Smith believes that vaccines applied during disease will be rarely, if ever, life-saving, but they may hurry a stationary or languid process which tends toward recovery, by bringing into play the unused reserves of various tissues. The article is a valuable one and is very sane in its consideration of the proper application of vaccine treatment both for prophylactic and curative purposes.

Autogeneous Vaccines in the Treatment of Chronic Joint Affections (Arthritis Deformans and Gonococcal Arthritis).—HUGHES (*British Med. Jour.*, 1913, 2737, 1267) considers that so-called rheumatoid arthritis is a form of metastatic arthritis due to some primary focus of infection. The commonest foci of infection in Hughes' cases have been the teeth, especially pyorrhea alveolaris, the nose and naso-pharynx, chronic otorrhea, the lungs, as a bronchitis or bronchiectasis, the intestinal tract, especially in diseases associated with stasis, and leukorrhea. In all such conditions the offending organism or organisms should be isolated from the primary focus and an autogenous vaccine

should be given for one or two doses. This raises the phagocytic powers of the patient, and it is then time to give the infected region the needed local treatment. If possible the primary focus should be removed. The use of the vaccines is to be persisted in for long periods of time if one is to succeed in the treatment. Hughes believes that chronic gonorrheal arthritis is due to a mixed infection with the gonococcus and staphylococcus, both of which can be cultivated from the interior of the urethra. A vaccine containing 100,000,000 gonococci and 150,000,000 staphylococci up to 500,000,000 of the former, and 1,000,000,000 of the latter is to be used, and after the second dose the chronic gleet is to be treated locally. Hughes has had very good results with this plan of treatment, but a complete cure often requires weeks or months.

The Diagnostic and Therapeutic Value of Intravenous Injections of "Arthrigonin."—Bruch and Sommer (*Münch. med. Woch.*, 1913, lx, 1185) have injected arthrigonin intravenously both for diagnostic and therapeutic purposes. Arthrigonin is a polyvalent gonococcus vaccine that has been used successfully by intramuscular injection in the treatment of gonorrheal epididymitis and arthritis, but is not of diagnostic value when given by this method. Bruch and Sommer have injected the vaccine intravenously for diagnostic purposes, giving 0.1 c.c. of vaccine diluted to 0.5 c.c. with saline to men and 0.05 c.c. or less to women and children. Gonorrheal patients always reacted within forty-eight hours by a rise in temperature of more than 1.6° C. Non-gonorrheal patients showed much less reaction. No severe local symptoms occurred. For therapeutic purposes increasing doses were given intravenously at three- to four-day intervals, beginning with 0.1 c.c. and gradually increasing to 0.5 c.c. of vaccine. The patients treated improved rapidly and no injurious effect was observed. Various gonorrheal processes were treated with good results. Bruch and Sommer conclude that arthrigonin given intravenously is valuable both for diagnosis and treatment of any infection due to the gonococcus.

The Newer Theories in the Dietetic Treatment of Diabetes Mellitus.—Tansz (*Med. Klinik.*, 1913, ix, 908) emphasizes the necessity of determining the point of tolerance for protein as well as for carbohydrates in each individual case of diabetes. In diabetes associated with nephritis, the diet should be regulated for nephritis as well as for diabetes and especially with regard to the tolerance for sodium chloride. The good results obtained from oatmeal and vegetable days is probably due to their increased alkali content and the consequent neutralization of acidosis. Tansz says that Abderhalden's researches have proved that albumin, fat, and carbohydrates develop protective ferments. Animal experiments have shown that it is possible for the body to produce ferments that aid in the splitting of the polysaccharides. In diabetes the metabolism is disturbed by an overaccumulation of carbohydrates, and if it were possible to increase the amount or the activity of soluble ferments the carbohydrates might be oxidized to a greater extent. Tansz says that experiments are being conducted with this idea in view.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

The Immediate Treatment of Depressed Fractures of the Skull in the Newborn.—KOSMAK (*Bulletin of the Lying-in Hospital of the City of New York*, March, 1913) reports four cases of immediate operation for depressed fractures of the skull in the newborn. He employs a hook six inches long, inside measurement 3.16 inches, the inner side flat and at right angle to the shank. The point of the elevating hook is carefully introduced and turned at right angles to the surface so soon as the inner table of the skull has been perforated, and with these precautions no injury to the brain substance will occur. The point of the hook must be sharp enough to readily penetrate the skin, which has been previously sterilized before operating. Fractures of the fetal cranium may result without instrumental interference, and so the head of the newborn child should be carefully examined in all cases where there is reason to suspect unusual pressure. In every case seen by Kosmak where there was a depression in the fetal cranium there was also a fracture. The effort to use manual pressure to raise the depressed bone has not, in the writer's experience, been practical or successful. Force may be applied by this method to such an extent as to cause intracranial hemorrhage.

The Wassermann Reaction and Tuberculin Reaction during Pregnancy.—In view of recent studies in the blood serum of pregnancy, it is interesting to note the behavior of the pregnant patient in the Wassermann reaction and that occasioned by the use of tuberculin. DAUNEY (*Archiv. mensuelle d'Obst.*, April, 1912) reports the results of his studies with the Wassermann reaction in 82 patients, and 57 infants born of these mothers. He finds evidence that pregnancy inhibits the action of the Wassermann test in syphilitic women, for the result of the test was much more feeble and less pronounced than in syphilitic non-pregnant patients. He also finds that antibodies pass from the mother into the milk, and, in examining newborn infants, he finds that one cannot predict the reaction of the child from the reaction given by the mother. Women in florid syphilis giving a positive reaction to the Wassermann test may give birth to children having no sign of syphilis, but yielding a positive or partial Wassermann reaction. Syphilitic women giving a partial Wassermann reaction may give birth to children in whom the reaction is much more pronounced, while syphilitic women giving a negative reaction may give birth to children in whom the reaction is positive. Women suspected of syphilis, but having no sign of a negative Wassermann reaction may give birth to children giving a positive reaction. In suspected cases, where the Wassermann reaction is but faintly positive, or doubtful,

the child may be markedly syphilitic. Where the Wassermann reaction is negative, the fetal reaction is often doubtful. Cases are sometimes seen where women without a sign of syphilis, but who are suspected only of the negative Wassermann reaction, may give birth to a child having florid syphilis. In 21 infants, the Wassermann test gave identical results in mother and child in 9 cases; in 12 cases the reaction in mother and child did not agree.

In the *Monatsschrift f. Geburtshülfe und Gynäkologie*, Band xxxvi, Festnumer, 1912, BAR gives his results in the cutaneous use of tuberculin with tuberculous pregnant patients. This test was used to determine the prognosis and indications for the interruption of pregnancy. He found that, where the results were negative or very feebly positive, prognosis must be reserved when the tuberculous lesions seem to be localized. If the patient grew worse, without regard to the test, the safer plan would be the induction of labor. In pregnant women with pulmonary tuberculosis, without well developed lesions and well-marked tuberculin reaction, one would not induce labor because the lesions were not grave. Where a second test with tuberculin gives a very positive result when the first test was negative, the indication would be that the tuberculous process was extending rapidly, and the pregnancy should be terminated. The negative reaction, which was negative after the birth of the child, in the presence of grave lesions would indicate an approaching fatal termination.

Ovarian Pregnancy with Full Term Fetus.—Such a case is reported by GRIMSDALE (*Jour. Obstet. and Gyn. of British Empire*, February, 1913). The patient was a multipara, the heart sounds of the mother regular, the heart not enlarged, and the general condition fairly good. Upon examination, a hard, freely movable tumor about the size of a melon could be felt in the lower abdomen, reaching to the umbilicus. The tumor was not tender, was dull on pressure, and there seemed to be no free fluid in the abdominal cavity. Upon vaginal examination, the uterus was to the right of the tumor and not connected with it. The diagnosis of a solid ovarian tumor was made, and at operation this was found freely movable, with but one small adhesion. When the tumor was removed from the abdominal cavity it was found to occupy the position of the left ovary. The left Fallopian tube and mesosalpinx were normal, and the left round ligament could be traced to the uterus, and lay at the right of the tumor. The specimen removed consisted of the left ovary with the left tube and mesosalpinx. Upon opening the tumor, it contained a fetus and the placenta. An ovarian pregnancy was undoubtedly present. The centres of ossification indicated that the fetus had reached term.

The Immunology of Pregnancy.—MURRAY (*Jour. Obstet. and Gyn. of British Empire*, February, 1913) has made experimental studies to determine the question of immunology of pregnancy. While he analyzes his results, it is remarkable how little of it has a bearing on the relation of the normal to the toxic. To obtain definite knowledge, further results from the epiphanin reaction must be obtained. It was observed that immunity reactions were no strict measure of the immunity developed. With a proved immunity reaction in preg-

nancy, it is clear that all harmonal interactions, such as thyroid insufficiency, can be relegated to a secondary position. Toxic pregnancy naturally represents a defect in the production of the protective factors. Abderhalden's experiments appear to indicate that the prime error is in the placenta. The eclamptic placenta is unquestionably more toxic than the normal organ, although there is no positive evidence of a primary abnormality. The placenta, however, is almost as rich in enzymes as the liver. The indications are that in toxic pregnancy something is lacking which can be supplied by the addition of healthy pregnant sérum, but in this the important element is the fresh character of the serum.

PETRI (*Zentralbl. f. Gynäk.*, 1913, No. 7) gives the results of his observations from the biologic diagnosis of pregnancy. He employed the blood serum from 23 pregnant hospital patients, and, by Abderhalden's method, made about 300 tests. These embraced all the months of gestation and the puerperal period after labor and abortion as well. He found the reaction positive as late as fourteen days after confinement. In 5 cases, it was positive from the first to the second day after abortion, and, in 9, from the first to the eighth day. He employed coagulated placental connective tissue obtained by boiling or cooking the placenta from which the blood had been removed.

Ileus Complicating Pregnancy and the Puerperal Period.—VAN DER HOEVEN (*Zentralbl. f. Gynäk.*, 1912, No. 46) has collected 94 cases of ileus complicating pregnancy and the puerperal period, and in 70 of these the histories give the cause, the treatment, and the prognosis. Adhesions were the cause in 35, and, of these, 24 were operated upon, with 13 recoveries and 11 deaths. The 11 which were not operated upon all died. Invagination was responsible for the accidents in 3 cases—1 operated upon, followed by death, and 2 recovering without operation. Volvulus was responsible for the condition in 13, 9 operations with 4 deaths, and 4 deaths without operation. Hernia in the anterior abdominal wall caused 2, 1 operated upon, followed by death, and 1 recovering without operation. Hernia in the broad ligament was the cause in 1 case cured by operation; in the mesentery in 1 case, dying after operation; in the diaphragm in 1 case, dying without operation. Epithelioma of the rectum produced 1 fatal case, without operation; stricture of the rectum, 1 of like nature; and ovarian cyst with twisted pedicle caused 3 cases operated upon, with recovery. Ovarian carcinoma was the cause in 1 case, recovering after operation. Posterior parametritis in 1, dying after operation. Hematoma in the pelvis caused 2, which recovered after operation; and retroperitoneal lipoma caused 1, dying after section. Incarceration of the retroflexed pregnant uterus was the exciting cause in 4 cases, 1 dying after operation, 2 dying without operation, and 1 recovering. Of 70 cases, 46 were operated upon, with a mortality of 46 per cent.; 24 were not operated upon, with a mortality of 81 per cent. In the remaining 24, constipation undoubtedly was the cause in 5; 1 of these died after operation, and 1 died without operation. In 15 fatal cases, autopsy failed to reveal any cause for the condition. Eight of these were not operated upon, and 2 died; 7 were treated by section, with 3 deaths. It is interesting to observe that even autopsy failed to reveal the

cause of the accident in between 15 to 20 per cent. of the cases. In view of the fact that many of these cases developed between the fourth and seventh month of gestation, and during the first day of the puerperal period, it seems impossible to believe that the pressure of the uterus on the intestine caused the condition. It is more rational to suppose that the pressure of the uterus against the bowel as it passes over the brim of the pelvis, was an important factor. When the vagina is not distensible at the third or fourth months as the uterus expands, traction is made upon the cervix, and the cervix is drawn up into the pelvic brim. This was well illustrated in a case treated by section in the third month of gestation. Contracted pelvis makes this pressure at the pelvic brim more pronounced, and the accident has occurred in these cases after delivery by symphysiotomy or Cesarean section. The presence of myomatous tumors of the uterus also predisposes.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Treatment of Uterine Hemorrhage by the Galvanic Current.—JAMOULLE (*Gaz. de Gynécol.*, 1913, xxviii, 49) says that uterine hemorrhages may be roughly divided into three groups, according to their etiology: (1) Those due to altered ovarian secretion, (2) those due to pathologic conditions of the endometrium, and (3) those due to alterations in the uterine *parenchyma*, *i. e.*, to atonia or insufficiency of the uterine muscle. The latter group, and these alone, are amenable to treatment by the constant galvanic current, the effect produced being dependent upon the well-known action of this form of electricity in causing contractions of smooth muscle. Cases of subinvolution, of profuse hemorrhage at puberty or the menopause, without demonstrable lesion, or associated with a sclerotic condition of the uterine walls, the result of long congestion or of chronic inflammatory processes, are the ones usually most benefited by the galvanic current; in these it appears to exert an excitomotor and trophic action upon the muscle fibres, whereby their tone is restored and their contractility increased. In a few cases of fibroid tumor, where operation is definitely contraindicated on account of tuberculosis, renal or cardiac conditions, the use of electricity may be justifiable, as well as in the case of patients near the menopause suffering with fibroid tumors, or of young women with small tumors, and desirous of having children. An absolute contraindication to this form of treatment is furnished by the presence of acute or chronic adnexal inflammation, since the excitation of the tubal musculature produced by it may lead to disastrous consequences. If the first electrical treatment is followed by a rise in temperature and pain in the adnexal regions, no further trials with it should be made,

even if the most careful palpation fails to reveal the presence of tubal masses. The technique is comparatively simple. Any ordinary medical battery furnishes the current. The positive pole consists of a sound of non-oxidizable metal (nickel, platinum), which is ordinarily introduced into the uterine cavity, and is surrounded by an insulating cuff to protect the vaginal walls. The negative electrode consists of a plate of metal wrapped in moist cotton, placed on the suprapubic region of the abdomen. A constant current is used, of from 50 to 60 milliampères; in rare instances this may be gradually increased to 150 milliampères. The sittings last from eight to ten, or occasionally fifteen minutes; they are given every other day, or even daily. As a rule, six to eight treatments are sufficient to produce the desired result. In some instances, expecially in hemorrhages of congestive nature, vagino-abdominal galvanization appears preferable, the positive pole being placed in the posterior vaginal vault instead of in the uterine cavity. In this case it is necessary to wrap it also in wet cotton, to avoid injury to the vaginal walls. In applying the treatment to young girls it is usually possible to avoid even intravaginal application, one pole being placed over the lumbar, the other over the pelvic region, a method which Jamoulle has found to give sufficiently satisfactory results in these cases.

Extirpation of the Bladder.—Two rather remarkable cases of almost complete resection of the bladder are reported by NICOLICH (*Folia Urologica*, 1913, vii, 371). Relying upon the work of Schwartz, who found that in dogs resection of the entire bladder except the trigone was followed by the formation of a satisfactorily functionating organ, Nicolich performed his first operation upon a patient, aged seventy-two years, who was suffering from a papillary, infiltrating carcinoma, involving the entire bladder wall with the exception of the trigonal region, which was free. After resecting the entire bladder, with the exception of this portion, he closed the peritoneum with cat-gut, and sutured it to the upper angle of his abdominal incision. He then brought the remaining portion of the bladder walls together as well as possible, but was not able completely to close the opening; a large tampon of iodoform gauze was, therefore, placed between the bladder and the peritoneum, and a second, smaller one directly over the bladder. The abdominal incision was left entirely open. The patient stood the operation well (spinal anesthesia); by the fifty-second day the wound had entirely closed, and micturition was normal, occurring about every three hours. Two months later the patient was able to return to work; a radiograph taken at this time, after the injection of 100 c.c. of collargol, showed the new-formed bladder in normal position, with a small diverticulum. Ten months after operation the patient was still enjoying the best of health. The second operation, practically identical in nature, was performed for multiple papillomas, which two previous cystotomies had failed to cure. In this instance the wound was closed by the twenty-second day; the patient urinated every two hours during the day and every four hours at night. A collargol radiograph two months later showed a somewhat larger and more regular cavity than in Case 1.

DERMATOLOGY

UNDER THE CHARGE OF
MILTON B. HARTZELL, M.D.,
PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

The Treatment of Carcinoma of the Skin with Carbon Dioxide Snow and the X-rays Combined.—FABRY (*Archiv f. Dermatologie u. Syphilis*, Band cxvi, Heft 2), finding that previous freezing of carcinomatous lesions lowers their resistance and makes them more readily influenced by the *x*-rays, employs the following combination in the treatment of such lesions, which he regards as superior to all other methods. The carcinoma is first frozen for one minute, then allowed to thaw completely and again frozen for a minute; it is then *x*-rayed immediately or after one or two days, four-fifths of an erythema dose being given. Under an indifferent salve healing takes place within two to four weeks, the length of time depending upon the size of the lesion. Of 12 cases treated in this manner complete healing was obtained in all but 1, in most instances with scarcely perceptible scarring.

The Experimental Production of Pellagra in the Monkey.—HARRIS (*Jour. Amer. Med. Assoc.*, June 21, 1913) has succeeded in producing in the monkey symptoms resembling human pellagra by employing subcutaneous, intravenous, and intracranial injections of a Berkefeld filtrate made from pellagrous human tissues. The first monkey injected remained apparently normal for many months, but eventually developed an eruption consisting of dark patches situated on the face, upper extremities, and trunk, and finally died with all the signs of pellagra. A second monkey which was given two injections two months apart, five months after the first injection showed scaly eruption of a dusky red color on the face, ears, and backs of the hands which itched. This monkey likewise developed a slight diarrhea and considerable salivation. Microscopical examination of the skin of the first monkey showed a picture identical with that presented by the skin in human pellagra. Harris believes the result of these experiments indicate that pellagra may be transmitted to the monkey by a Berkefeld filtrate made from pellagrous human tissue, and that the cause of pellagra is a filterable virus capable of passing through the Berkefeld filter.

A Tuberculide Resembling the Lichen Planus of Wilson.—VIGNOLO-LUTATI (*Annales de Dermatologie et de Syphiligraphie*, 1913, No. 4) reports the case of a woman, aged twenty-five years, who presented an eruption, situated exclusively upon the backs of the hands and the extensor surfaces of the lower third of the forearms, consisting of papules presenting the characters of lichen planus. The papules were pink or violaceous, with smooth shining surface, and in some instances showed a minute umbilication. The eruption was not accompanied by any subjective symptoms. The patient likewise presented the

symptoms of pulmonary tuberculosis and, in youth, had suffered from a scrofulous adenitis the scars of which were still visible in the neck. Microscopic examination of sections of excised lesions stained by the method of Weiss revealed a small number of tubercle bacilli. This case was in all essential features like the one reported by Bosellini, in which tubercle bacilli were also demonstrated.

Studies in the Metabolism of Some Diseases of the Skin.—Neiditsch (*Archiv f. Dermatologie u. Syphilis*, Band cxvi, Heft 1) studied a series of 41 cases of various diseases of the skin, such as psoriasis, ichthyosis, dermatitis, herpetiformis, dermatitis exfoliativa, acute and chronic eczema, urticaria perstans, urticaria pigmentosa, for the purpose of determining whether there was a greater increase than normal in the excretion of the amino acids, *i. e.*, whether there was a disturbance in albumin catabolism, regarding these acids as the most characteristic elements of the albumin molecule. His investigations led to practically negative results, since in none of these diseases neither—in psoriasis, eczema, nor ichthyosis, could an increase, of pathogenetic significance, be demonstrated; nor was the quantity of amino-acids contained in a spontaneous bleb of pemphigus vulgaris increased. Geber (*Dermatologische Zeistschr.*, Band xxii, Heft 5, 1913), in a study of the nitrogen and sulphur metabolism in psoriasis found, contrary to the conclusions of Haemerli recently published, that with a constant weight of nitrogen there was no increase in the excretion of sulphur in psoriasis. The variations in the sulphur excretion which he observed in his cases stood in close relationship to the increase or diminution of nitrogen intake. Although an increase in the sulphur excretion in proportion to the intake was noticed with a nitrogen-poor diet, he did not regard this as at all characteristic of psoriasis.

Mycosis Fungoides Successfully Treated by Hypodermic Injections of Arsenic.—Wolff (*Archiv f. Dermatologie u. Syphilis*, Band cxv, Heft 9) at a meeting of the Strassburg Dermatological Society, December 15, 1912, exhibited a case of mycosis fungoides which had been successfully treated by injections of atoxyl and arseniate of soda. The patient was a man, aged thirty-three years, who, in 1907, had an eruption scattered over the whole body consisting of irregularly-shaped, elevated, partly scaly, partly papillomatous areas with polycyclic borders, accompanied by moderate itching. After seventy injections of atoxyl (dose not mentioned) complete healing took place, and the patient remained well until 1910 when two lesions appeared upon the chin like those above described together with a fungoid tumor with broken-down centre upon the sole. Injections of arseniate of soda in ascending doses up to 0.03 per day, with *x*-ray treatment of the foot, produced complete healing in six weeks. The exhibitor also presented photographs of two other cases of mycosis fungoides successfully treated in the same manner.

Erythema Nodosum and Tuberculosis.—Pollak (*Wien. klin. Woch.*, 1912, No. 32) in 48 cases of erythema nodosum occurring in children obtained a positive tuberculin reaction in every case. He is therefore of the opinion that erythema nodosum is probably a

tuberculous affection of the skin. SEZARY (*Medical Press and Circular*, 1912) calls attention to the fact that many children with tuberculous meningitis have previously had an attack of erythema nodosum.

Multiple Pigmented Warts in Pregnancy.—WARD (*British Jour. Dermat.*, May, 1913) records an unusual and annoying complication of pregnancy. A healthy brunette, aged twenty-three years, became pregnant for the first time, and in the later months of her pregnancy was greatly annoyed by the appearance of a crop of pigmented warts on the trunk, neck, and limbs; with the termination of the pregnancy a few of the warts disappeared, but the majority remained. Four years later the patient again became pregnant, and at the end of the fifth month a new crop of warts appeared over the body and extremities, avoiding the face and hands. Unlike in the previous pregnancy, none of the warts came off with the birth of the child.

The Treatment of Epithelioma of the Lip by the X-rays.—PUSEY (*Jour. Cutaneous Diseases*, February, 1913), while not advocating the substitution of the *x*-rays for radical surgical measures in the treatment of epithelioma of the lip, believes that, in selected cases it is capable of producing results which compare favorably with those obtained by purely surgical methods. In support of this opinion he presents the following statistics: From 1901 to 1909, 44 private cases of epithelioma of the lip were treated by the *x*-rays. Six of these are for various reasons left out of consideration, leaving 38 cases, 35 of the lower lip, and 3 of the upper. Of these 38 patients 28 were living and well in January, 1912. Two of the patients had lived nine years; 7, eight years or more; 7, seven years or more; 5, six years or more; 2, five years or more; 5, four years or more; and 8, three years or more. The percentage of failures was only 5.25.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL.

The Action of Arsenic in the Anemic.—SANEYOSHI (*Zeitschr. f. Path. u. Ther.*, April, 1913, xiii, 1) details his observations in pursuance of the knowledge of the way in which arsenic acts on the cure of anemia. He has observed the morphological changes in the blood of dogs during the administration of arsenic, and by oxygen-estimation, the degree of regeneration; finally he has compared the iron content of the liver and spleen with the normal. Arsenic in large toxic doses causes hemolysis and a corresponding anemia, for the repair of which regeneration at once proceeds. In smaller doses,

though still relatively larger than those in ordinary therapeutic use, no anemia occurs, and no marked change is to be observed in the blood. There appeared no unusually rapid disappearance of corpuscles nor any unusually prompt replacement of such corpuscles as had disintegrated. Oxygen analysis verified these observations, and forms a very accurate mode of estimating the variability of young corpuscles in the circulating blood. No regeneration beyond normal limits seemed to occur, nor was hemosiderosis demonstrable in the liver and spleen. Bettmann, and later, Kuhn, consider that arsenic does not directly stimulate the blood-forming organs but causes a peripheral hemolysis, and the consequent lack of oxygen becomes or causes the stimulus to bone-marrow. Saneyoshi thinks this untenable, but does not go further than to suggest that arsenic is especially potent upon cells that are young and strongly proliferative.

Experimental Myocarditis from Rheumatic Sources.—Bindo de Vecchi (*Arch. de Med. Exper.*, xxiv, 352) undertook the blood examination of rheumatism, but found his cultures from the blood stream to be sterile. He then injected the serum of such blood intravenously in dogs and rabbits; to the naked eye this was followed by no result, but microscopically there resulted areas of cellular infiltration, of general distribution, but most evident in the papillary muscle, and chiefly perivascular. The cells are sometimes of one kind, sometimes of various sorts, lymphocytes, leukocytes, and plasma-poor cells with large nuclei; subsequently fibriotic processes appear. Four cases out of five showed these areas, which were never found in control animals. Blood from persons sick of nephritis, polyneuritis, and tuberculosis showed lymphocytic areas with slight muscular degeneration; but the author has not regarded them as specific, as are the areas under consideration. They bear great likeness to the so-called "rheumatic nodules" observed in the heart muscle of persons dead of rheumatic fever. Their situation in the myocardium makes it seem probable that extension could readily occur to endocardium and pericardium. De Vecchi's next step would naturally be to use the Berkefeld filter upon such serum, and to verify his interesting observations by larger series of animals.

Recurrent Fever.—During the course of study upon exanthemic typhus, Nicolle, Blaizot, and Conseil (*Annal. de l'Inst. Pasteur*, March, 1913, xxvii, No. 3) were enabled to make some interesting observations with regard to recurrent fever, namely, that it is transmitted by lice. It may be said with regard to exanthemic typhus that the local name in Tripoli is translatable as "the louse disease," a term which has its purpose in an attempt at prophylaxis. The louse has for some time been suspected of being the transmitter of recurrent fever, and the chief reason against admitting the truth of this supposition was that lice nourished upon men or apes suffering from disease were unable to cause the disease in others by biting. When examining lice which had bitten patients suffering from recurrent fever, it was found that there was a rapid disappearance of the spirilla from the body of the insect; but prolonged observation showed that this disappearance is only apparent, for after a delay of eight days

they reappeared and persisted for a couple of weeks before they again disappeared finally. The spirilla after their reappearance are virulent for man and ape. They are localized to the lacunar cavity, and do not invade the apparatus of the mouth or the digestive tube. Shut off from communication from the outside, as long as the louse remain alive, they perish with the death of the insect. A simple bite does not, therefore, infect. One victim, whether human or Simian, had as many as 6500 bites inflicted upon him without becoming infected. It is when the body of the louse is crushed and the skin excoriated by the nails at the same time, that the lacunar liquid escapes, and inoculation occurs. The head louse and the body louse are both efficient causes of the disease. The infection is preserved, doubtless, through the various generations of the insect, and each variety of acarus has apparently its own variety of spirillum.

Transplantation of Tumors upon an Embryo.—J. B. MURPHY (*Jour. Exper. Med.*, April 1, 1913, xvii, No. 4) has obtained some wonderfully striking results in inoculating rat-sarcoma into developing chick embryos. It is at the present time difficult to correlate all the various observations that have been made tending to show the specific nature of tissues in their behavior one to another. There was recently shown in the *Journal of Experimental Medicine*, by Rous, a striking example of the strictness of the laws of specificity; chicken sarcoma failed to grow in any other chickens than blood relations of the host in its first transfers; later it would grow in any animal of the same breed, and ultimately, when its malignancy had been much enhanced, it would grow in chickens of other breeds. Some have supposed that there is in the body of the host an immunity reaction against the foreign cells; others have thought that the host lacks some specific food substance which is necessary for the growth of the grafted material. Briefly, Murphy was able without difficulty to obtain tumors in the embryos, or in the membranes, and was able to carry the inoculation from embryo to embryo indefinitely. During long life in a new host, the rat cells showed no change in their morphology, nor any loss in their ability to produce characteristic tumors when transplanted back into the rat. When placed in the adult chicken tissues, the embryo-nourished cells died even more quickly than cells taken direct from the rat, so that they appear to have gained no adaptation to the new species. Murphy has succeeded in implanting various embryonic cells from the chicken, mouse, and rat, as well as various other sarcomas, chondromas, and carcinomas, upon the embryos.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

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